Non-toxic tumortherapy (NTT) for advanced colorectal cancer with liver metastasis, a pilot study

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Summary
Eighty-three patients with livermetastases from colorectal cancer and in many cases also metastases elsewhere consulted me in 1988-1997 for non-toxic tumortherapy (NTT). No selection was made. Two regressions during only NTT-therapy were seen. This is significantly more than expected. Median survival time of patients receiving 5-FU with or without leucovorin (14.5 months) was better than expected, comparing with historical controls. So the results clearly indicate patients' lives were prolonged by NTT.

Keywords : orthomolecular, colorectal, cancer, 5-FU, Leucovorin and metastatic/metastasis.

Introduction
Metastases to the liver from colorectal cancer do mean a bad prognosis. Median, one year and two year survival differs considerably, however, due to selection and different therapies applied.
Patients with 4 or fewer metastases in the liver and no metastases detectable elsewhere are often operable, although in more recent times also patients with more metastases in the liver are operated upon (1). The overall survival of metastasectomy of hepatic colorectal metastases ranges in general from 20-40% (2). See also Bolton et al (3). In Pubmed-searches more and more adjuvant chemotherapy is seen after metastasectomy for colorectal liver metastases. The patients in this study came into my practice between 1988 and1998. They had synchronous liver metastases or the metastases developed after potential curative colorectal surgery and a number of them had also metastases elsewhere. The majority (51%) received neither chemotherapy nor 5-FU, eventually combined with leucovorin (LV).
What is the (median) survival of non-treated patients with liver metastases from colorectal cancer and what is the (median) survival of patients with such metastases treated with 5-FU (and LV)? Finan et al (4) studied 90 patients and found a median survival for non-treated patients with synchronous liver metastases of 10.3 months; they, however, excluded 2 patients dying within 2 weeks from the study on unscientific grounds and the article does not say anything, unfortunately, about including or excluding patients with also extrahepatic metastases. De Brauw et al (5) followed a group of 83 patients with colorectal cancer and liver metastases; 3 had resection of the liver metastases and 24 received 5-FU; median survival was 8.4 months. Balslev et al (6) followed a group of 188 patients with cancer of the rectum or rectum sigmoid and synchronous metastases in the liver; 5 had treatment for liver metastases; the other 183 were not treated: they had a median survival of 6 months and only one survived for longer than 37 months. Luna-Perez et al (7) analyzed retrospectively 77 patients with liver metastases from colorectal cancer. Patients treated with 5-FU and leucovorin had a median survival of 15 months and patients not treated with chemo had a median survival of 13 months (the numbers were respectively 32 and 45). In the study of Luna-Perez et al patients with extra hepatic metastases were excluded, however, this explains their good results. For patients with hepatic metastases from colorectal cancer Purkiss and Williams (8) found a median survival of 125 days; for patients with only metastases in the liver median survival was 175 days and for patients with extrahepatic disease median survival was 92 days.
An impression of the median survival times can also be found in some randomized studies. Abad et al (9) found in advanced colorectal cancer (not always liver metastases) with 5-FU plus LV a median survival of 12.6 months and with only 5-FU , a median survival of 7 months. 5-FU with a low, respectively high dose of LV, gave median survivals of respectively 9.3 and 10.7 months in advanced colorectal cancer (10).
Under Results and Discussion many other studies will be mentioned to make a clear analysis of the results of this study.
The aim of this pilot-study is to find out, in spite of the limited number of patients, whether NTT (non-toxic tumortherapy) can cause a regression in patients with liver metastases of colorectal cancer and more relevant can prolong life. NTT means nutritional therapy with supplements, herbs, thymus-extracts, etc. Here I will only give an introduction to NTT. In my book written in Dutch: "Voedingsinterventie bij kanker "(Nutritional Intervention in Cancer) (11), more recent factors are discussed, as well as factors giving in the adjuvant setting, a better chance to cure patients from colorectal cancer.

The supplements, herbs etc. used in this study are mentioned briefly here, with of course the most recent literature. Omega-3-fatty acids from fish oil inhibit growth of coloncancer in animals (12,13,14). In humans with end stage malignant disease fish oil with vitamin E prolongs survival in a randomized study significantly (15).
In a randomized study mistletoe prolongs the lives of patients with metastasized colorectal cancer significantly (16).
Vitamin D (fatty fish, fish oil, sunshine) is also interesting. People diagnosed with colon, prostate or breast cancer have a better prognosis when the cancer is diagnosed during summer or fall, the seasons with the highest vitamin D-levels (17). In accordance with this is the inverse correlation between serum levels of 25-hydroxyvitamin D3 and stage of colon cancer (18). Vitamin D3 also promotes differentiation of colon carcinoma cells in vitro (19). So there is a ratio for vitamin D in the treatment of cancer.
Thymostimulin gives significant more regressions by 5-FU plus LV in advanced colorectal cancer (20) and also less mucositis and diarrhoea from 5-FU and LV. This raises the question: do oral preparations work, too, with patients with advanced colorectal cancer? In this study I administered injections with thymus, but mostly only an oral preparation.
L-selenomethionine inhibits in vitro the growth of colon cancer cells (21, 22); possibly by inhibiting the transcription of COX-2 (22). Selenite enhances in vitro the antitumoractivity of 5-FU, irinotecan and oxaliplatin against colon cancer cell lines (23). Selenite also causes differentiation and apoptosis in vitro in human colonic carcinoma cells HT29 ; glutathion seems to potentiate this (24).
Calcium spirulan derived from Spirulina platensis inhibits tumor invasion and metastasis of colon carcinoma cells in vitro (25).
Quercetin by itself and in combination with the heat shock can induce apoptosis and necrosis in vital human colon adenocarcinoma cells (LS 180) (26). Quercetin inhibits in vitro growth of colon cancer cells by inhibiting lactate efflux (27) and also by binding to a estrogen receptor (28). Quercetin chalcone inhibits also growth of a colon tumor implanted in Balb-c mice (29).
Vitamin C alone does not prolong survival of patients with advanced colorectal cancer in two randomized studies (30); Moertel et al, however, administered the placebo longer and they gave the less favourable alkaline form (11). Vitamin C, however, potentiates the anticancer activity of 5-FU in vitro (31). So overall vitamin C has the benefit of the doubt. In any case the best established effect of vitamin C against cancer is the fact that vitamin C with copper causes a burst of free radicals that can destroy cancer cells (11).
Beta-carotene induces in vitro apoptosis in a colon carcinoma cell line (32,33). Beta-carotene inhibits rectal ornithine decarboxylase activity in colon cancer patients (34); this suggests beta-carotene has als therapeutic activity in colon cancer.
Low retinol-plasmalevels in colorectal cancer are correlated with a poor response to chemotherapy (35) and the metabolite retinoic acid induces in vitro differentiation of colon cancer cells (36).
DHEA inhibits in vitro growth of colonic adenocarcinoma cells by depletion of mevalonate (37). Moreover DHEA potentiates in vitro the anticancer effect of 5-FU against colonic adenocarcinoma cells (38).
EGCG (epigallocatechin-3- gallate) derived from green tea inhibits topoisomerase 1 in vitro in colon carcinoma cells; this makes EGCG a candidate for a therapeutic application (39). EGCG inhibits colon and other cancer cells in vitro but not their normal counterparts (40). See also (41).
Melatonin inhibits growth of colon cancer in vitro and in animals (42). Melatonin used next to a low dose of irinotecan gives a good therapeutic result in colon cancer patients; as good as with a high dose of irinotecan alone (43). Melatonin also prolongs in randomized research, the lives of patients with advanced cancer, among them many with colorectal cancer (44).
Curcuma longa (extract), containing curcumin is a COX-2-inhibitor (45); it is likely for curcumin to inhibit cancer growth in this way although there are at least 9 other relevant mechanisms (11).
Indeed curcumin inhibits also growth of colon cancer cells in vitro (46, 47). In a phase-1-trial in 15 patients with advanced colorectal cancer, refractory to chemotherapy, stable disease for 2-4 months was seen in 5 patients. The doses used were relatively low : 440-2200 mg Curcuma a day (=36-180 mg curcumin a day); no side effects were seen (48). I advise 1800 to 3600 mg Curcuma extract a day.
GLA (gamma-linolenic acid) inhibits growth of colon cancer in vitro (49). Invasion of colon cancer cells is also inhibited by GLA in vitro (50). In a randomized study in partly patients with an advanced colorectal cancer prolonging of life was seen with 2500-3000 mg gamma-linolenic acid in the form as primrose oil (51).
Ginsenosides inhibit metastasis of colon cancer in mice (52). In a randomized study in patients with rectal cancer ginseng induced apoptosis, causing palliation of symptoms like frequent defecation, tenesmus and hematchezia (53).

Consumption of tomatoes is linked to a reduced rate of colorectal cancer (54). Furthermore, in several animal models a very significant reduction of colorectal cancer by tomato juice and by lycopene is discovered (55). It is tentative to suggest lycopene has also therapeutic activity in colorectal cancer. Anyhow in 2 randomized trials a therapeutic effect against prostate cancer was found (56, 57).
Coenzyme Q10 reduces, probably by immunostimulation, the induction of colon cancer in rats by dimethylhydrazine (58). There is no research with Q10 in patients with advanced colon cancer. Q10 has however already shown to have some anticancer activity in animals with cancer (59) and also in advanced breast cancer (60, 61, 62). It would be interesting to try Q10 also with patients having advanced colorectal cancer.
Berberine has an anticachectic effect in mice bearing a colon carcinoma by inhibiting IL-6 production (63).
Lentinan from Shiitake mushrooms inhibited growth of inoculated colon cancer cells in mice; Lentinan was orally administered in this experiment (64). Lentinan can even give regression of peritoneal carcinomatose with rats (65). In animals (mice) Lentinan also makes colon cancer more sensitive to cisplatin (66). In several trials prolonging of life in patients with advanced colorectal cancer by Lentinan is seen; see for example Taguchi T (67).
Resveratrol (found mainly in grapes, wine etc.) inhibits in vitro colon cancer cell growth by apoptosis-induction (68). Resveratrol also potentiates induction of differentiation in CACO-2 colon cancer cells by butyrate (69).
Silymarin prevents azoxymethane-induced colon carcinogenesis in rats to a high extend (70). Silymarin inhibits in vitro growth of colon cancer cells; anti-angiogenesis appears to be in this case an important mechanism (71). Silymarin is also able to inhibit colon cancer growth in vitro by induction of apoptosis (72).
Probiotics mixture inhibits in vitro the induction of colon cancer by azoxymethane (73). Lactobacillus casei inhibited in mice the growth of a secondary implanted colon cancer after resection of a first implanted colon cancer (74). In my book (11) one can find several randomized studies, in which Lactobacillus casei shows a clear activity against already existing cancer (bladder, lung and cervical cancer).
Beta-sitosterol inhibits in vitro growth of colon cancer by apoptosis ; see for example (75).
Soja consumption seems associated with a slightly reduced rate of colon cancer; in experiments with rats soy-protein and not genistein, reduced the number of azoxymethane induced colon cancer (76). In neither another experiment with rats did genistein reduce the incidence of azoxymethane induced colon cancer (77). Existing colon cancer cells are, however inhibited in their growth by genistein; apoptosis by genistein is in this respect an important mechanism (78, 79, 80).
S-allylmercaptocysteine (SAMC) , a compound from garlic, inhibits in vitro growth of colon cancer (81, 82).
PSK (Polysaccharide-K) from Coriolus versicolor as an oral adjuvant has shown to improve survival in patients operated for colorectal cancer Dukes B/C (11, 83). In vitro PSK inhibits the growth and invasion of several colon cancer cell lines (84). In vivo PSK caused by intraarterial administration, a regression in one out of seven patients with liver metastases from colorectal cancer was seen (85). In animals this has been found more explicitly (85). So the mycoceuticals Lentinan and PSK are very interesting for use in the treatment of advanced colorectal cancer. Maitake is also interesting (83). There are clearly favourable effects on the immune system and there exist anti-tumour effects as well (83). For example: in vitro prostate cancer cells are inhibited in their growth by an extract of Maitake, causing apoptosis (86). More research on Maitake in relation to (advanced) colorectal cancer is needed.
The germanium compound Ge-132 inhibits growth of lung cancer in mice directly after inoculation. Administering Ge-132 after an operation on a large tumor of this kind had no effect, however (87). Dozono et al (88) found Ge-132 to give considerable relieve of pain in terminal cancer patients. More research on Ge-132 would be interesting.
NAC (N-acetyl-l-cysteine) reduces the number colorectal cancer in rats with chronic ulcerative colitis (89). In mice treated for adenomatous polyps NAC suppresses the proliferative index in the colon (90). NAC is able to inhibit in vitro colon cancer cell growth by suppressing type 1 insulin-like growth receptor expression on these cells (91) (and in this way reducing stimulation of cell growth bij type 1 insulin-like growth factor).
Folic acid has a consistent negative correlation with colorectal cancer (92). Moreover, folic acid is able to induce in vitro inhibition of EGFR tyrosine kinase activity in colon cancer cells and so their growth (93). The favourable interaction of the active form of folic acid (Leucovorin) and 5-FU is well known; see e.g. (94). Leucovorin and 5-FU will be discussed in greater detail under Results and discussion.
Ursodeoxycholic acid reduces, in a randomized placebo-controlled trial with ulcerative colitis and primary cholangitis patients, the combined number of colorectal dysplasia and colorectal cancer significantly (95). Ursodeoxycholic acid inhibits in vitro proliferation of colon cancer cells by apoptosis (96, 97).

Artemisinin induces in vitro apoptosis in cancer cells and so inhibits their growth (98). In rats dihydroartemisinin and ferrous sulfate retarded fibrosarcoma growth (99). So Artemisia annua extracts have anticancer activity; research regarding colorectal cancer would be interesting.
Polyerga, glycopeptides of the porcine spleen, inhibit development of lung metastases in mice with a mammary carcinoma. In the Polyerga-group survival is significantly better (100). Polyerga also inhibits development of melanoma-metastases in the lung in mice (101). In a randomized study in patients with advanced head and neck cancer with Polyerga Borghardt et al (102) saw fewer side effects of chemotherapy (cisplatin/carboplatin, 5-FU). In spite of there being no research, concerning colorectal cancer, I gave this to many patients with an advanced colorectal cancer.
Cimetidine potentiates in vitro antiproliferative effect of 5-FU against colon carcinoma SW620; this was not the case, however, when 5-FU was applied against the SW620 derived doxorubicin resistant cell line SW620, Ad300 (103). Cimetidine itself also inhibits the growth of 2 other colon cancer cell lines in vitro and also in vivo (104). Also in an earlier stage cimetidine is useful: in rats given 1,2 dimethylhydrazine colon cancer incidence is lower and the growth of the colon carcinoma is inhibited (105). In mice the growth of colon cancer implants is also inhibited by cimetidine ; an important effect here was angiogenesis inhibition by cimetidine (106). In a randomized trial in patients with advanced colorectal cancer 5-FU gave with cimetidine a higher response rate than with 5-FU alone (107).
Alpha-lipoic acid can cause in vitro apoptosis in cancer cells, not in normal cells (108). In vitro alpha-lipoic acid is especially cytotoxic to leukaemic cell lines (109). There is, however, no proof alpha-lipoic acid has a relevant effect against colorectal cancer.
Coumarin inhibits in vitro the growth of Caco-2, a colon cancer cell line (110).
D-limonene inhibits growth of colon cancer in vitro and in animals (111).
Bromelain (from pine apple) inhibits metastasis of Lewis lung cancer in mice (112) and also inhibits e.g. invasive capacity of glioma cells in vitro (113). Bromelain is interesting although no research on bromelain and colorectal cancer has been done.
Pycnogenol locally applied on the skin of mice, protects against inflammation, immuno suppression and carcinogenesis induced by UV radiation (114). Pycnogenol seems to have therapeutic effects also: it induces in vitro selectively, apoptosis in human mammary cancer cells (115).
Shark cartilage delays carcinogenesis in mice (induction of renal cancer by streptozotocin) (116).
Shark cartilage does not inhibit, however, growth and metastasis of the SCCVII carcinoma in mice (doses from 5 to 100 mg per mouse) (117). In a phase I/II trial with shark cartilage in sixty patients having an advanced carcinoma no complete or partial regressions were seen; there was also no indication either comparing with historical controls, shark cartilage prolongs life (118). U-995 derived from shark cartilage inhibits growth of sarcoma-180 in mice and metastasis of a melanoma in mice as well (119). So shark cartilage is a very speculative anti-cancer agent, certainly for humans with an advanced colorectal carcinoma. Clearly bovine cartilage is also a speculative agent to treat cancer patients with.
Calcium reduces the risk of colorectal cancer (120). It is not known whether calcium has an inhibiting effect in colorectal cancer, although there are indications this is possible (121).
Amygdalin, a cyanogenic glycoside showed in vitro and in vivo anti-tumor promoting activity in mice (122). Beta-glucosidase (sets free cyanide from amygdalin) bound to a bladder cancer associated monoclonal antibody combined with amygdalin has a clear anti-tumor activity in vitro (123). In animals amygdalin had no influence on anti-tumor activity of cytosine arabinoside, methotrexate, 5-FU and others (124). In animals with or a Ridgway osteosarcoma, or a Lewis lung cancer or a P388 leukemia, amygdalin alone or in combination with beta-glucosidase had not any significant anti-tumor effect (125).
In another study (126) the same is found in animals with leukemia or a B 16 melanoma or a carcinosarcoma. Human breast and colon tumor xenografts in athymic nude mice were not inhibited in their growth by amygdalin (127). Two other leukemia's were also not inhibited in mice by amygdalin (128). A phase I trial in 178 people with advanced cancer amygdalin did not cause any regression or stabilization (129). In this trial, however, amygdalin was only used a few times on at the patient's request.
Bromelain most likely exerts its anti-cancer activity by peroxydase activity (112). This makes the use of glutathionperoxydase containing supplements a logic thing as done in a number of cases in this study.

Beta-lapachone from LaPacho inhibits in vitro the growth of HCT-116 colon cancer cells by apoptosis (130). In vitro vitamin K1 antagonizes the antineoplastic activity of LaPacho and of lapachol (a constituent of LaPacho) (131); so anti-vitamin K activity might be an antineoplastic propertie of LaPacho in vivo. Beta-lapachone from LaPacho inhibits in vitro topoisomerase I and II and also poly(ADP-ribose)polymerase; all these enzymes are essential for the integrity of DNA; a fact is that beta-lapachone inhibits in vitro the growth of colon, prostate, ovary and breast cancer cell lines (132). NAC, vitamin C and vitamin E inhibit by antagonizing elevation of H2O2-production in vitro growth by beta-lapachone (133). Genistein potentiates in vitro apoptosis by beta-lapachone in prostate cancer cells (134). In rats lapachol inhibits the growth of Walker carcinosarcoma (135). In a phase I trial with nine advanced cancer patients three complete regressions were seen, but three of these nine patients had to stop the therapy because of nausea and vomiting (136).
The reason to give in general a multi (not containing vitamin K) is to prevent major deficiencies and also to prevent (further) metastasis; especially important for patients operated upon for liver metastases (137).
L-cysteine intake must be adequate for L-glutathione biosynthesis (138). Moreover it is likely extra L-cysteine just like NAC potentiates 5-fluorouracil (139): it seems that reduction of intracellular levels of reactive oxygen species enhances susceptibility to 5-FU.
Iodine-deficiency is a risk factor for thyroid, breast and stomach cancer (11, 140). Iodine rich sea weed inhibits the development of breast cancer in animals (141, 142). Moreover, in rats inorganic iodine is able to inhibit growth of existing DMBA-induced breast cancer (143). So iodine has also therapeutic properties ; this has already been suggested by Cornelis Moerman, Dutch' first orthomolecular physician in the fourties of the last century (144). So it is speculative to give iodine to patients with advanced colorectal cancer, but ther are, as is clear, arguments to do so.
PB-100 a substance from Pao Pereira, inhibits in vitro growth of BCNU-resistant astrocytoma cells but not of normal astrocytes (11, 145). Flavopereirine (=PB100) from Pao pareira inhibits in vitro DNA-synthesis of different types of cancer cells not the synthesis of normal DNA (11, 146). In this study Pao pareira-extracts, however speculative, were given to a number of patients. Alstonine from Rauwolfia vomitoria also inhibits in vitro synthesis of cancer DNA, though not the synthesis of normal DNA (146). Alstonine has been shown to have antitumor activity in vivo: the transplantable YC8 lymphoma and the Ehrlich ascites tumor in mice were curable with alstonine in a number of cases (147). In this study alstonine has also been given to a number of patients.
Factor AF-2 is an extract of embryonal sheep liver and spleen (11). In a randomized study it diminishes the side effects of adjuvant chemotherapy in breast cancer patients and although there were significantly more patients in the AF-2-group estrogenreceptor negative, the number of relapses within 30 months was non-significantly lower in the AF-2 group (148). In a randomized study with patients having advanced breast cancer, AF-2 reduced the side effects of adriamycine/cyclofosfamide (149). In a randomized study with urothelial carcinoma patients in an advanced stage factor AF-2 reduced the side effects of chemotherapy with cisplatin and methotrexate (150). Also the side effects of cisplatin plus epirubicin (for hormone refractory prostate cancer) and FEC plus Leucovorin (for intestinal tumors/gynecological cancer) respectively were reduced in randomized studies (151 and 152 respectively). In some individual cases colleagues have seen regressions with factor AF-2; among these cases was one colorectal cancer (148). So AF-2 has been used in some patients on a speculative basis. The side effects of chemo that are reduced by AF-2 are myelo suppression and nausea/vomiting.
Ayur Vedic herbs, MAK-4, can inhibit in animals the development of breast cancer (153). Whether these herbs can inhibit progression of advanced colorectal cancer is uncertain. The Ayur Vedic herbs combination MAK-5 induces in vitro differentiation of neuroblastoma cells and in this way inhibits their growth (154). The ethanol-extract of MAK-4 inhibits in vitro growth of human, but not of mouse melanoma cells (155); an ethanol-extract of MAK-5 in this study induced differentiation in human but not in mouse melanoma cells, although the growth of both melanoma types were inhibited in vitro.

Despite the limited evidence in this study a number of patients got Ayur Vedic herbs (MAK-4 and also MAK-5).
A number of patients received next to vitamin C Fe3+ in a glucose-solution in accordance with Moerman (144); the idea was: cancer cells take up preferentially glucose and so maybe also Fe bound to glucose; Fe3+ would become Fe2+ and Fe2+ would, together with vitamin C, induce a burst of free radicals killing the cancer cell; for this model there is no clear proof however.
Furfural was also given to a limited number of patients because it can inhibit lactate excretion by the cancer cell (156). Furfural cannot be recommended for prevention because under extreme conditions it can promote the development of cancer (157, 158).

Patients and methods

This is a prospective study in which all patients (eighty three) with advanced colorectal cancer and at least metastasis in the liver (in fact a form of negative selection) entering in my practice from the beginning of 1988 untill the end of 1997 are included.

They had liver surgery and/or chemotherapy with 5-FU, in a number of cases combined with leucovorin; in one case topotecan was chosen ; or no regular therapy after diagnosis of metastasis. Shortly after the diagnosis of advanced colorectal cancer with at least one or more metastases in the liver the patients came to see me. Liver surgery was done as fast as possibly; if operation was impossible, chemotherapy was often postponed as long as possibly or omitted. If the tumor relapsed after liver surgery 5-FU with leucovorin was also applied in some cases. In table 1 we see the patient chacteristics and also the regular therapies they received.

Table 1. Patient Characteristics and regular therapies chosen

Male/female	46 / 37
Age at moment of diagnosis liver metastasis	
< 50 years	16
50-69 years	56
70 years or more	11
median (range)	59 (25-77)
5-FU (with LV)	41
without metastasectomy	38
with metastasectomy	3
no chemo	42
without metastasectomy	38
with metastasectomy	4

The Diet Recommended

The diet recommended was a mixture of the Meditarenean and Japanese diet. This mixture of diets has a lot in common with the so called Moerman-diet (11, 144, 159, 160). The following main guidelines can be given:

a. As much fruit and as many vegetables and/or juices derived from these as possible. Especially citrus fruits, carrots, broccoli, spinach, tomatoes, onions, avocado's and pineapple were recommended.
b. Brown rice or whole-meal paste and leguminous plants (quite often fermented soy products) were preferred over potatoes.
c. Fatty fish (not smoked) was advised three times a week. Herring, salmon, mackerel, tuna, sardines, sea eel and sea devil were especially recommended.
d. Leavened bread made from wheat and/or rye without extra fat was recommended.
e. Milk-products: only low fat milk-products, containing living lactobacilli, were permitted to a maximum of 0,5 litre a day.
f. Cheese: only young cheese prepared without a fungus and no more than 40 grams a day.
g. No meat.
h. Nuts and seeds: walnuts, almonds, pumpkin seeds, sesame seed and linseed. No maize and peanuts. Walnuts, almonds and linseed are especially preferred because of their high content of omega-3-fatty acids.
i. Mushrooms: Shiitake and also Maitake were especially recommended.
j. Oils and fats: for heating, only olive oil was recommended. For salads olive oil with a little linseed oil was recommended. The use of pumpkinseed oil, walnut oil, soybean oil and sesame oil was permitted. The use of corn oil, sunflower oil, peanut oil and safflower oil was discouraged. Only a minimal amount of butter (on bread) was allowed.
k. Herbs and spices: garlic, curcuma, rosemary, carawayseed, cumin, saffron and ginger were especially recommended. Parsley, basil, oregano, coriander, thyme, cloves and sage were recommended to a lesser extend. Nutmeg and redundant salt were discouraged.
l. Sugar: no (white) sugar; only minimal honey.
m. Drinks: green tea and licorice tea were recommended; black tea was discouraged. One or two cups of regular coffee a day were allowed. The only alcohol allowed was one glas of dry red wine a day.

Supplementation
Eighty of eightythree patients used a multi (65 one One Daily, 7 one or two Orthobasis and 8 two Dagravit 30 totaal per day).One daily: for composition see reference 159 ; for composition of orthobasis go to www.orthos.nl; for the composition of Dagravit 30 totaal; see 161.

Almost all patients ate fatty fish and took linseed oil ; some took only linseed oil. Cod liver oil was used by 61 of the 83 patients; the average daily intake of these 61 patients was 2.1 table spoons a day. An average is always calculated for the group that is using the supplementation; not for the whole group. The remaining 22 patients took besides the multi, a vitamin D supplement: 7 took alfacalcidol: 0,25-1 mcg daily and 15 took 1,25-dihydroxyvitamin D3 : 500-4000 IU a day (only one patient took 1500 IU and 1 without taking cod liver oil 4000 IU; the remaining 13 patients took 500-1000 IU vitamin D3 a day).

Vitamine E (in general a natural form) was supplemented next to the vitamin present in the multivitamins (respectively 100 IU, 66.7 IU and 1 mg vitamin E). A number of patients also used one and sometimes more than one capsule of ortho oxydant (see below), containing 73.5 mg vitamin E per capsule. Vitamin E sec was used by 67 of the 83 patients in doses from 150 to 600 IU per day (average 343 IU per day). Taking into account the multi and the ortho oxydant, all patients got extra vitamin E ; one patient got only 2 mgs extra per day; all the others at least 100 IU per day extra.

Vitamin A was supplemented very often. The idea was : the liver accumulates vitamin A and that might give an intense local anti-tumor effect. Vitamin A supplementation was taken by 79 of the 83 patients (50000-250000 IU a day; average 140000 IU per day). Multi vitamins contain also some vitamin A and cod liver oil contains a considerable amount (about 15000 units per table spoon); this has of course also to be taken into account. Only two patients had a supplementation below 15000 IU a day (both about 3000 IU a day).

In 50 of 83 patients beta-carotene was supplemented in doses ranging from 15 to 150 mgs a day (average 76 mg). Ortho oxydant (see below), however, contains also beta-carotene (15 mg per capsule) ; 46 patients took 1 ortho oxydant in general. So in total 67 patients got beta-carotene in doses ranging from 15 to 150 mg (average 69 mg a day).

Four patients used 15-30 mg lycopene for a certain time.

NAC 2 times 600 mgs a day was used by 7 patients.

Ortho oxydant ; composition : 15 mgs synthetic beta-carotene ; 300 mgs vitamin C; 300 mcgs L-selenomethionine , 100 IU vitamin E , 30 mgs L-glutathione , 50 mgs L-cysteine , 50 mgs L-glycine and 50 mgs L-glutamic acid. It was used by 46 patients (1-3 capsules a day; average: 1,2 a day); 2 of them were also using NAC.

Seventy-six patients used supplemental selenium: 6 used L-selenomethionine 500 up to 2000 mcgs a day ; 71 used sodiumselenite (1000 up to 5000 mcgs a day). The average intake of the whole group on the basis of this separate selenium supplementation was 2300 mcgs selenium a day. The multis contained 10-200 mcgs L-selenomethionine and some patients also took ortho-oxydant (see above). Taking all the supplements together only one patient only received 10 mcgs selenium extra a day; another only 200; all the other patients had in total 500 mcgs selenium a day or more.

L-glutathione-complex (158 mgs L-cysteine, L-glutamic acid 194 mgs, L-glycine 98 mgs and 50 mgs L-glutathione per capsule) was used by 24 patients; 1 to 20 capsules were used a day (average 5,25 capsules a day); 9 of these patients also used ortho oxydant and 3 of the 24 patients also used NAC. Only one patient used ortho oxydant, L-glutathione-complex and NAC.

Fifty seven patients took extra vitamin C besides ortho oxydant (300 mgs vitamin C) and the multi (20-150 mgs vitamin C). Besides the two preparations mentioned these patients took 1-7.5 grams of vitamin C extra (average 2,3 grams a day). Fourteen patients received neither extra vitamin C as such nor 1 or more ortho oxydant. Only two patients did not receive any supplement with vitamin C (no multi, no ortho oxydant and no vitamin C as such).

Extra iron as Fe3+ in a sugar solution (exact dosage not known to me anymore) was taken by 6 patients 1-3 times a day (average 2,5 times a day). Except one patient (taking Fe3+ only once a day) these patients took extra vitamin C. The multis also contained extra iron (Fe2+) per pill: One Daily 14 mgs ; Orthobasis 3,3 mgs and Dagravit 30 totaal 15 mgs.

Fifty patients took 500 mgs calcium/250 mgs magnesium 1 or 2 times (38 one and 12 two pills).

Besides the very modest amounts of folic acid in the multi (400 mcgs or less) 10 patients took 5 to 15 mgs folic acid (average 8 mgs). Leucovorin, the active form of folic acid used in combination with 5-FU was of course used in much larger quantities.

Fourteen patients took 3 grams of primrose oil daily and two took 4 grams of primrose oil daily.

Six patients took 300-360 mgs silymarin daily (average 350 mgs a day).

Seventeen patients took Panax Ginseng Meyer-extract G2001 120 mgs 1-3 times a day (on average: 212 mgs a day).

Twenty patients took 3-25 mgs of melatonin before going to sleep (average : 11,5 mgs a day).

Sixteen patients took 200-600 mgs DHEA a day; average 375 mgs a day.

Lactobacilli were taken, in general, in the form of fermented milk products; 12 patients also had supplemented Lactobacilli as one or two capsules Biodophilus N111 (contains 1 billion Lactobacillus acidophilus INT9 and 1 billion Bifidobacterium bifidum per capsule; see www.orthos.nl) after meal.

Fifty-four patients took a Shiitake-supplement, i.e. one to six capsules a day (average: 3 capsules a day; composition per capsule (a 6:1-extract: derived from in total 7,2 grams of mushroom): 200 mgs Shiitake; 300 mgs Cordyceps; 300 mgs Hakumokuji; 200 mgs Reishi and 200 mgs Maitake).
One of the fitfty-four and one other patient took also KSM-itake 3 times 4 capsules a day; composition: Optam 30 mgs; sulindac 3 mgs and 267 mgs of a mixture of Coriolus versicolor, Shiitake and the Maitake-D-fraction ; more information on www.mierlohout.nl.

Sixty patients received thymus extract as oral supplement; two of them also had thymus injections as well as five other patients not taking oral thymus extract. So 65 of the 83 patients got thymus. The thymus capsules were delivered by Orthogland (Thymus-G620; see : www.orthos.nl/aov/orthogl.htm); the patients mentioned took 2-6 pills a day (average 4,5 a day).
The thymus-injections were done with Thym-uvocal (see: www.orthos.nl/aov/aovprod.htm): 2 times 2 mls were injected i.m. each week.

Nine patients took 170-510 mgs genistein a day (average 370 mgs a day).

Thirty-two patients took 3 to 6 polyerga capsules a day (average: 4,7 capsules a day).

Twenty-one patients took 30-60 mgs of coumarin; one patient took 105 mgs of coumarin daily; average intake among these twenty-two patients was 44 mgs a day.

Twenty-eight patients had factor AF-2 as described in literature twice a week.

Only one patient used 400 mgs cimetidine 3 times a day.

One patient used Ge-132 earlier from another physician for a longer time; dosage not known.

One patient used d-limonene 6 ml a day for several months.

One patient used ursodeoxycholic acid 3 times 300 mgs a day for several months.

Eleven patients took quercetin (found in large amounts in onions, tomatoes, red wine, apples etc.;11) .
Doses varied from 3 times 1 to 3 times 3 capsules of 200 mgs a day. On average they took 1145 mgs a day.

Also only one patient got resveratrol supplementation (75 mgs a day).

Thirty-one patients took Q10 in doses ranging from 15 mgs to 200 mgs a day (average: 76 mgs a day).

One patient took 20 mgs pycnogenol 3 times a day.

Only one patient took 2 grams curcuma longa a day extra as a supplement.

Three patients took EGCG as a supplement: i.e. respectively 1, 6 and 12 capsules a day with 150 mg EGCG a capsule.

Bromelain was taken by 2 patients; respectively 300 and 600 mgs daily. Two other patients took respectively 1 and 3 caplets a day, containing per caplet 76000 IU SOD, 18000 IU catalase and 460000 IU L-glutathioneperoxydase.

Seven patients used 1000 mcgs iodine next to the iodine from the multivitamin (150 mcgs of One Daily or considerably less), fatty fish and cod liver oil.

Twenty-nine patients took 1-12 spirulina pills of 300 mgs a day (average: 6.2 pills a day) ; the iodine content of these algae is very low.

Pao pereira was used by 18 patients: they took 2-12 capsules (300mg/30% flavopereirine) a day during chemotherapy ; excluding the two patients with the lowest and the highest intake. Intake varied from 3-6 capsules a day; average intake of the group was 5.1 capsule a day.

Twelve patients took a teaspoon of MAK-4 twice a day and eleven of them took two pills of MAK-5 a day.

Rauwolfia vomitoria-extract was used by one patient: 300 mgs extract with 11% alstonine 3 times a day.

Three patients took a few milligrams berberine a day; this is probably too little to have an anticancer effect in vivo. Based on animal experiments, 600 mgs a day seems needed (162).

Only one patient took SAMC (derived from garlic); the daily intake was about 3 grams a day of a highly enriched extract.

Seven patients took 6 500 mgs capsules of a LaPacho-preparation a day, although 2 of them also took a multi containing vitamin K (Orthobasis).

Artemisia annua was used by 4 patients: they took 1 capsule containing an Artemisia annua-extract 250 mg/25% twice a day.

Only 2 patients used 100 mgs alpa-lipoic-acid a day.

Nine patients took 6-20 grams of Vitacarte, derived from cowcartilage (average 14 grams) daily for a certain period because of further progression of the disease. For the same purpose one other patient took 18 grams shark cartilage daily for some time.

Six patients used a non-toxic amount of furfural (1-3 capsules a day) for a certain period; the exact dose is not tracebale any longer.

Amygdalin was used by 5 patients: 1000-1500 mgs a day.

The statistical methods applied are described under Results and discussion.

Results and discussion

Two very remarkable patients

I will discuss two patients showing a (partial) regression after starting NTT.
The first patient is a woman born 09-03-1919. In 1988 colorectal cancer with livermetastasis was discovered. CEA was 51, liverfunctions were clearly increased, the liver was 6 cms enlarged and she was losing blood with the stools almost every day. I advised her the more classical Moerman approach. She went on the diet and in addition she had to take one tablespoon cod liver oil daily; 50000 IU of vitamin A 3 times a day; the Fe3+-solution 3 times a day (temporarily and apart from selenium); 2 grams of vitamin C twice a day; B-complex plus 2 dagravit 30 totaal; 600 IU vitamin D daily; vitamin E 400 IU daily; 500 mcgs L-selenomethionine 3 times a day plus 1000 mcgs sodiumselenite twice a day; 30 mgs beta-carotene daily; temporarily 2 L-glutathione-complex 3 times a day (no Fe3+ in the same period); folic acid 5 mgs a day; Q10 30 mgs a day; 15 mg coumarin with some troxerutin twice a day and alpha-lipoicacid 100 mgs once a day. She never received chemotherapy.
In about one year : the CEA went down from 51 to 6; blood loss with the stools stopped; liver functions became normal and accordingly the enlarged liver became no longer enlarged on palpation. In the second year the tumor gradually came back and 2 years after diagnosing colorectal cancer with liver metastases this patient died.
The second patient is a man born 04-05-1927. He already had chronic lung disease and a bypass in 1991. In November 1992 he was diagnosed with colorectal cancer and operated upon. As fast as one month later 3 liver metastases were observed. He saw me and got the following supplements/medicines: NAC 600 mgs three times a day; one One Daily; 400 mgs of magnesium a day; vitamine C as calciumascorbate: 3 grams a day; natural beta-carotene 120 mgs a day; retinol: 117000 IU seperately a day; one table spoon of cod liver oil a day; vitamin E 200 IU a day; oral thymus-extract 5 capsules a day before meals; quercetin 3 times a day 500 mgs; spirulina 1 tablet a day; Shiitake complex 2 times 1 a day; alfacalcidol (etalpha) 0,25 mcgs twice a day; i.m. factor AF-2 twice a week and also for a certain time 1 gram of calcium plus 500 mgs magnesium a day.

He followed this regimen for somewhat more than fifteen months, but went off this therapy after a serious stroke. He did not have any chemotherapy. During the NTT 2 of the three metastases of the liver disappeared. In November 2002, about ten years after the diagnosis of colorectal cancer with metastasis to the liver, the patient died from cardiovascular disease, one week after his son died from esophageal cancer.
After the regression of the metastases it was asserted afterwards these metastases were in fact haemagioma's. This is not only afterwards, it was also impossible to find in relevant literature examples of regression of haemangiomas without giving any symptoms. Rupture plus internal bleeding is possible in principle, that is true, but there was no indication for this to happen twice in this patient.

Two regressions among the patients not receiving 5-FU with or without LV is too much of a coincidence. Moreover, with a comparable, although less advanced dietary approach at least 2 regressions of such colorectal cancers had been seen in the Netherlands before (described in reference 144: cases 5 and 28; in the first patient the tumor started growing again after stopping the nutritional therapy). The chance of a spontaneous regression of an inoperable (metastasized) colorectal cancer is low: as mentioned in reference 144 , over a period of 60 years seven cases of spontaneous regression of colorectal cancer were reported bij Everson and Cole (163). No cases were found in the Netherlands, although several cases from elsewhere were described in the years after 1966. In the eighties and the beginning of the nineties of the last century about 10 percent of the cancer patients used a nutritional diet on orthomolecular basis (144); as described in reference 144 the 2 cases referred to were too much to be a coincident.
In my group of 83 patients two cases of regression or even one among fewer than 83 (patients with a regression during 5-FU with or without LV could in fact not to be assessed) is also too much to be a coincidence: in Holland in 2003, 9898 patients were diagnosed having colorectal cancer while 4405 patients died from colorectal cancer (see www.kwfkankerbestrijding.nl). In the period in which my patients were ill the numbers cannot be markedly different. So in the actual ten years of my research about 40.000 patients died from colorectal cancer in Holland. So one would have expected on basis of the incidence of 1/40 (as in this article), about 1000 spontaneous regressions assuming NTT has no sense. This was clearly not the case. Outside the NTT-circuit no cases of spontaneous regression were seen in Holland. Another way of calculation is as follows. The number of cases worldwide was in 1990 about 782000 (see www.studentbmj.com : Peter Boyle and Michael JS Langman , both from the University of Birmingham have written an article entitled : ABC of Colorectal Cancer : Epidemiology). Less than nine spontaneous regressions are seen in the literature during the ten years mentioned, so the incidence of spontaneous regression is less than one in 700000. So in my group we had a chance to find one spontaneous regression of 700000/80 = 1/8750. So 2 cases of spontaneous regression are more than expected. If we add the cases described in reference 144, it is clear NTT can cause regression in patients with advanced colorectal cancer. The question is also, what is the mean advantage of NTT? So median survival and long term survival should be evaluated.
I did not see many regressions of advanced colorectal cancers in later years (I saw one): the explanation is simple: chemotherapy for advanced colorectal cancer changed from a very disputable therapy to a standard one. So regressions (mostly) take place during chemotherapy, even if not caused by chemotherapy.

Median survival of the whole group and the subgroups and also the long term survival of the whole group.

The whole group had a median survival of one year and 19 days. After 1 year 51 % was alive and after 2 years this was 23%. Five patients (6 %) were alive at 5 years. Comparing with the mixed group of de Brauw (5): a median survival of only 8.4 month's, this is a good result.
The group receiving 5-FU with or without Leucovorin: the 41 patients had a median survival of 14.5 months. In the group 3 patients were operated upon liver metastasis; after a relapse they received 5-FU with or without Leucovorin and all the three of them survived longer after the new relapse than the median survival time of the whole chemotherapy group.
The group receiving no 5-FU with or without Leucovorin and including 4 patients with metastasectomy of the liver (3 cases succesful in the long run): 42 patients had a median survival of 8 months. When, in this case we only take into account the patients having neither 5-FU +/- LV nor operation (38 patients) median survival was 7 months and 6 days. If we take into account the references 6,8 and some other literature I came across this is a good result. I found however too little literature to make the same statistical approach as I will do for my 5-FU with or without Leucovorin-group.

Of the seven patients that had a metastasectomy: 5 survived for 5 years or more. Three of these were really cured (alive after respectively more than 10 years). This is also a relatively speaking result; see references 1, 2 and 3.
Let us now have a look at the group receiving 5-FU with or without LV, compared with (historical) controles from literature. First a description of literature studies.
Martoni et al (164) treated patients with metastasized colorectal cancer with 5-FU plus LV or without LV. Both groups consisted of 32 patients. The median survival of these groups was respectively 10 and 7 months.
Abad et al (9) found a median survival of 7.5 months in 34 patients with only 5-FU and a median survival of 12.3 months in 75 patients with 5-FU and LV.
Buroker et al (10) compared 5-FU plus a low dose of LV and 5-FU plus a high dose of LV in patients with advanced colorectal cancer. There were 2 groups containing about 181 patients. Median survival was respectively 9.3 and 10.7 months.

Di Costanzo (165) found median survival times of almost 14.3 and 12.3 months in respectively 87 and 88 patienst with respectively 5-FU and 5-FU plus LV.
Steinke et al (166) found median survival times of respectively 6.5 and 9 months in 63 respectively 59 patients treated respectively with 5-FU and 5-FU plus LV.
Labianca et al (167) found median survival times of 11 and 12 months respectively in 90 respectively 92 patients with advanced colorectal cancer with 5-FU and 5-FU plus LV respectively, .
Petrelli et al (168) gave patients with advanced colorectal cancer (respectively 113,115 and 115 patients) 5-FU or 5-FU with a low respectively high dose of LV. Median survival times were respectively 10.5, 12.75 and 10.75 months.
Valone et al (169) compared 5-FU to 5-FU plus LV in 55 respectively 107 patients. Median survivals were respectively 11.2 and 11 months. A group with 5-FU, LV and methotrexate (103 patients ; had a median survival of 11.7 months).
Ehrlichman et al (170) compared 5-FU to 5-FU plus LV in respectively 63 and 61 patients. Median survival times were 9.6 and 12.6 month's respectively.
Petrelli et al (171) compared 5-FU with 5-FU plus LV and with 5-FU and methotrexate. The groups of 58 patients each had median survival times of respectively almost 12 months again almost 12 months and 10.5 months.
Bobbio-Pallavicini et al (172) compared 5-FU to 5-FU plus LV in respectively 50 and 100 patients. Their median survivals were respectively 6 and 8 months.
O'Connell (173) compared 5-FU to 5-FU with a low/high dose of LV. The number of patients in the groups was respectively 60, 76 and again 60 patients. The median survival times of the groups were respectively 7, 11.5 and 11.5 months.
Nicholas et al (174) compared 5-FU (22 patients) to 5-FU + low LV and methotrexate (22 patients) and with 5-FU and high LV (30) patients. Median survival times were 12 months or somewhat less.
Nobile et al (175) compared 5-FU with 5-FU plus LV in respectively 45 and 50 patients. The respective median survival times were 10 and 9 months.
Leichmann et al (176) tried 3 variations in 5-FU with or without LV in 3 groups with respectively 170, 178 and 173 patients. Median survival times were respectively 14.5 , 14 and 13.5 months.
Aranda et al (177) compared 5-FU plus low-dose LV with 48-hours continuous infusion of 5-FU in respectively 153 and 153 patients. The median survival times were 10.75 and 11 months.
Borner et al (178) compared 5-FU and 5-FU plus LV in 2 groups of 155 patients. The respective median survival times were 10 and 12.4 months.
Kalofonos et al (179) compared 5-FU to 5-FU plus LV and to 5-FU plus interferon in groups of about 64 patients. The respective median survival times were 14.7, 16.3 and 12.4 months; the median survival time for the whole study population was less than 14.5 months.
Schilsky et al (180) compared 5-FU plus elinuracil with 5-FU plus LV in respectively 485 and 479 patients. The respective median survival times were 13.3 and 14.5 months.
Kohne et al (181) compared 5-FU plus LV with 5-FU plus interferon and with 5-FU plus interferon/LV in respectively 91, 90 and 49 patients. Median survival times were respectively 16.6 , 12.7 and 19.6 months.

Perez et al (182) followed 445 patients with metastatic colorectal cancer. They all were treated with 5-FU plus LV; some also underwent secundary surgery of the liver and or lungs. Median survival time was 18 months. Three, five and ten year survivals were 17.9 , 4.5 and 2.4% respectively. Long term survival at 3, 5 and 10 years in my chemotherapy group was 9.5 , 6 and 1.2%. As regards all 83 patients in my practice 9.6 , 6 and 3.7% were respectively alive after 3,5 and 10 years. Overall survival of my patients, while only 41 got 5-FU with or without LV, is overall even non-significantly better in the long term, although the patients alive after 10 years had had besides NTT, only operation of the liver.
The median survival time in the Perez group is an extremely good result compared with my group (median survival 14.5 months), but in my group secundary liver/lung operations were not done and 5-FU was often given to my patients in a low dose and mostly without LV. So this article is excluded from the analysis described below.
To weigh the median survival of the chemotherapy group I will compute the median survival for each relevant reference. The total number of patients of all relevant references with a median survival time for the whole group less than 14.5 is computed; the same will be done with the other relevant references. The two results are 4.727 and 230 patients. The sum is 4.957 patients. So my rough estimation of a one-sided P-value attributable to my chemotherapy group is about 0.048 (230/4.957). I also made an rough estimation of the overall median survival of the references referred to, by multiplying median survival of every subgroup and the number of that subgroup, adding these results and dividing the total by 4.957. The result is 12.0 months.

A search for articles whether median survival time during 5-FU-therapie will be significantly better when LV is added gave additional interesting information. Ehrlichmann et al (183) gave 126 patients 5-FU plus1-leucovorin. Median survival time was 12.5 months. Marsh et al (184) compared two different applications 5-FU plus LV combined with methotrexate in 168 patients. Median survival times were 15.3 and 11.4 months (overall less than 14.5 months).
Scheithauer et al (185) combined 5-FU, LV and cisplatin in 59 patients. Median survival time was, however, only 11.5 months. Laufman et al (186) found a median survival time of 8 months in 46 patients with 5-FU plus LV and Machiavelli et al (187) combined 5-FU, LV and trimetrexate in 36 patients with advanced colorectal cancer. Median survival time was 11 months. Although I did not find that time proof LV having influence on median survival time of patients with advanced colorectal cancer, these 5 publications with a median survival time of less than 14.5 months confirm the previous result.The chance that 5 publications, if comparable, all have a shorter median survival time than my chemotherapy group is of course smaller than 0.5 to the power 5 = 1/32. This means again my chemotherapy group probably had a longer median survival time than expected.
My patients were treated by NTT, but not in the most perfect way (no internet in my practice before 1997). A lot that was published, was not known to me. E.g. almost all patients received fish oil and vitamine E, but most did not get mistletoe, although both were tested positively in randomized research (see respectively 15 and 16).
I compared with especially trials starting with patients in a relatively good condition. In some publications all patients also received LV. The majority of my chemo-patients did not receive LV and all had at least metastases to the liver. Finishing this article I found what I did not find before : a recent meta-analysis showing 5-FU plus LV prolongs median survival of patients with advanced colorectal cancer significantly more than 5-FU alone : 10.5 months with 5-FU alone and 11.7 months with 5-FU and LV (188). So in my research, there were at least 3 kinds of negative selection, in fact, strengthening my result.
My book (11) with about 1700 references updated a lot; internet (pubmed) helped me a lot too. In 2000 I started a list of randomized studies concerning NTT. Chapter 2 of my book is based on about 100 randomized studies. Now we have a list of almost 1100 randomized studies on www.kanker-actueel.nl (look under : Onderzoek en voeding). Ten years ago I saw 4 regressions of cancer in general a year with NTT ; nowadays I see about 20 of such regressions a year.
A description of the individual combinations of medicines/supplements has not been presented, because a multi variate analysis is questionable because it would be more a subgroup-analysis with too much coincidence owing to the low numbers of the subgroups.
The final conclusions of this pilot study are that NTT causes more regressions in metastatic colorectal cancer than is expected on basis of coincidence. Median survival time of patients receiving 5-FU with or without LV is also longer than is expected on basis of controls of literature, although the result is modest.
The results are in line with other research in the field of NTT (see for example 144 and 159).
The explosion of facts from randomized studies concerning NTT in general, supported by internet will in my opinion improve results in the future. The effect for example of PSK as an adjuvant therapy (In stage Dukes B/C a 15 percent higher cure rate !! ; 11, 83) is impressive and now PSK has been applied in Holland for 7 years by NTT-physicians (not by regular medicine).
I intend to repeat this study for the years 1998-2007.

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