

## Research Article

# A Study on the Influence of Spirituality on the Efficacy of Antitumor Therapies with Natural Anticancer Agents in Untreatable Metastatic Cancer Patients

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## Abstract

The recent discoveries of the existence of natural anticancer agents either from plants, such as Aloe, Myrrh and Magnolia, or from the human body, namely the pineal hormones, allowed the possibility to elaborate new therapeutic natural combinations as a link between the commonly used palliative and curative cancer therapies, which would have not considered in a separate manner. The present study was carried out to evaluate the influence of the spiritual status on the efficacy of a natural anticancer combination containing pineal anticancer hormones in association with Aloe, Myrrh and Magnolia extracts in a group of 70 untreatable metastatic solid tumor patients with life expectancy less than 1 year. The spiritual sensitivity was evaluated by an appropriate faith test for patients affected by an untreatable disease. The percentages of both objective tumor regressions and disease control obtained in patients with high faith score were significantly higher with respect to those found in patients with low faith score. On the same way, the 3- year percent of survival achieved in patients with high faith score was significantly longer than that found in the other group. This study would suggest the efficacy of an antitumor therapeutic strategies with natural anticancer agents also in metastatic cancer patients form whom no other standard antitumor treatment was available, with a greater efficacy in the presence of a real status of spiritual faith.

**Keywords:** spirituality, cancer disease, psychoneuroimmunology

## Introduction

Being cancer a biological war between a human host and an apparently unconscious tumor mass, it is obvious that the prognosis of the neoplastic diseases may depend on both tumor characteristics and the psychobiological identity of cancer patients. Tumor characteristics regard histology, disease extension, biological grading and eventual genetic mutations of cancer cells. At the other side, the individual identity of the single cancer patients involves their consciousness status, psychological behaviour, life style, but also and mainly their endocrine, neuroendocrine and immune status in addition to their clinical conditions [1]. Until some years ago, the human diseases were considered to be due to organicistic or psychosomatic reasons. On the contrary, with the progressive advances in the area of Psychoneuroendocrinoimmunology (PNEI), it was understood that the psychospiritual status of patients may influence the biological body not only through the nervous system, but also through complex nervous, neuroendocrine and endocrine interactions with the immune cells, which after their activation may interact with the endocrine and nervous systems by releasing immunomodulating proteins, the so-called cytokines, which are also able to exert neuroendocrine effects by realising complex feed-back circuits between neuroendocrine and immune systems [2].

As far as the psychological and spiritual point of view is concerned, must be remarked that until few years ago and yet up to now by most researchers, the spirituality has been simply considered only as a part of the psychological status of humans, and only recently some preliminary clinical investigations have suggested that the spirituality is a different condition from both psychology and religion [3]. As far as the relation between psychology and spirituality is concerned, it is possible to affirm that the Psychology represents the analysis of the emotional life, which has its energetic matrix in the sexuality, whereas the Spirituality regards the reality of the different consciousness states. At the other side, the relation between Religion and Spirituality, according to a definition previously reported in the literature [4], the Spirituality is the research of the ultimate meaning of life, while Religion is only a set of beliefs and ritual practices within a well defined religious institution, then it would simply represents one of the possible ways to realize own self spirituality, even though more widely followed with respect to an individual manner to live and feel the spiritual dimension. Then, the individual spirituality may be realized through the same religion or other mysticai experiences, and it Is not a simpie set of emotions, but it constitutes a status of consciousness. Moreover, in agreement with PNEI discoveries [5], both emotions and consciousness states require a well defined psychoneuroendocrine mediation. Then, from a clinical

point of view, the two major problems concern the identification of adequate methods to clinically investigate not only the religious profile of patients, but also their spiritual sensitivity, as well as of possible eventual blood biochemical parameters able to reflect the psychological and spiritual status of patients and its influence on the clinical course of the neoplastic disease. However, most studies carried out up to now have been generally limited to the investigation of the influence of the personal religion rather than the real status of cancer patients. In any case, even though limited to the investigation of the influence of religion on the prognosis of cancer, preliminary clinical results seem to suggest that the religious support may allow an increase in the survival time of advanced cancer patients and to improve their clinical status, even though through still unknown mechanisms [3, 4]. The recent advances in PNEI knowledgements, by demonstrating that the immune responses *in vivo* are physiologically under a psychoneuroendocrine modulatory control [6,7], which represents the biochemical mediation of the spiritual and psychological status of the patients, may allow the hypothesis that the spiritual status may influence the clinical course of the neoplastic disease and the efficacy of the different antitumor therapies by stimulating the immune system and piloting it in an antitumor way through the activation of well-defined psychoneuroendocrine circuits [8]. Moreover, it has to be considered that until about 20 year ago, almost all scientific investigations in the oncological area were limited to the identification of possible carcinogens in the nature, either endogenous molecules, such as estrogens and androgens, or exogenous substances, capable of inducing the malignant transformation. On the contrary, more recent researches have demonstrated the existence of several antitumor plants containing well characterized anticancer molecules, in particular aloe hemodin from Aloe [9], guggulsterone from Myrrh [10] and honokiol from Magnolia [11], as well as more surprisingly the evidence of anticancer endogenous molecules, which would be responsible for the natural immunobiological resistance against cancer onset and growth, in particular some indole hormones released by the pineal gland, namely melatonin (MLT) [12] and 5-methoxytryptamine (5-MTT) [13], and the great group of beta-carbolines [14], which are mainly produced by pineal gland itself. All those natural anticancer agents has no important toxicity. Therefore, the existence of both endogenous and exogenous anticancer agents with a complete lack of biological toxicity but with well known antitumor properties, would justify their employment in the medical Oncology in an attempt to realize a link between the simple palliative and the curative therapies of cancer, since several anticancer natural agents, according to the PNEI knowledgements, may deserve both palliative and antitumor effects on cancer progression at least in terms of survival time. The present study was performed to investigate the influence of the spiritual status of consciousness on the antitumor efficacy of a psychoneuroendocrine regimen with antitumor pineal hormones in association with the most investigated anticancer plants in a group of metastatic solid tumor patients, for whom there is no other standard effective therapy of their tumor, by evaluating the spiritual status through a previously described clinical test to explore the spiritual faith in patients affected by an untreatable disease [15].

## Materials and Methods

The study included 70 untreatable metastatic solid tumor patients. Eligibility criteria were, as follows: histologically proven metastatic solid neoplasm, measurable lesions, no availability of standard antitumor therapies because of progression on previous chemotherapies, age or low performance status (PS), and life expectancy less than 1 year. Patients affected by metastatic breast cancer or prostate carcinoma were excluded from the study, because of the availability for those tumors of well tolerated hormonal therapies also by the standard medical Oncology. The faith test for patients affected by an untreatable disease employed in the study was performed by the observation of the clinicians in an attempt to exclude possible unconscious mental manipulations in their answers by the patients, and it consisted of the analysis of five major criteria [15], by assigning 20 points to each single criterion, with a maximum score of 100 points and by defining the presence of a real status of spiritual faith for a minimal score of at least 60 points or more. The five criteria were, as follows: 1) complete self-consciousness by the patients of the severity of their diagnosis and prognosis in terms of life expectancy: the absence of an adequate knowledge of the severe prognosis would transform the faith in a simple illusion; 2) lack of excessive anxiety: the anxiety would represent the opposite mental condition with respect to a real spiritual faith; 3) lack of an exaggerated attribution of value by the patients to the professional capacities of the single clinicians, being their disease as considered as untreatable on the basis of the standard medical therapies; 4) lack of an excessive analytic tendency by the patients to understand the chemical mechanisms involved in the efficacy of treatments instead of their significance in terms of reactivation of an effective biological natural anticancer resistance; 5) perception of own neoplastic disease not only as a personal problem, despite pain and other intolerable symptoms, but also as an individual manifestation of a general universal suffering involving all humans. The clinical characteristics of patients are reported in Table 1. Lung cancer, pancreatic adenocarcinoma and colorectal cancer were the neoplasms most frequent in our patients. The PNEI strategy of cancer cure consisted of the oral administration of the two most investigated anticancer pineal hormones, MLT and 5-MTT, in association with a phyto-therapeutic regimen consisting of the administration of extracts of the most investigated antitumor plants, including Aloe *arborescens*, Myrrh and Magnolia. MLT was given at 100 mg/day during the dark period of the day, while 5-MTT was administered at 5 mg in the early afternoon. Magnolia cortex, with a honokiol content of at least 50%, was given at 500 mg twice/day. Finally, Aloe and Myrrh were given at a dose of 10 ml twice/day of a mixture of 60% Aloe and 40% Myrrh. Patients with brain metastases also received *Boswellia* at 1000 mg/day in the morning, because of its anti-oedema effect. The clinical response was assessed by the WHO criteria by repeating the radiological examinations at 3-month intervals. Data were statistically analyzed by the chi-square test. The survival curves were calculated by the Kaplan-Meier method and statistically analyzed by the log-rank test.

**Table 1.** Clinical characteristics of 70 untreatable metastatic solid tumor patients.

<b>CHARACTERISTICS</b>	
M/F:	37 / 33
Median age	65 years (range 43 — 92)
Median PS (ECOG)	1 (0—3)
<b>RELIGIOUS FAITH</b>	
- Specific religion:	29/ 70 (41%)
- Catholic Christian religion:	23
- Protestant Christian religion:	2
- Oriental Christian religion:	1
- Buddhism:	2
- Islam:	1
- No religion or undefined religion:	41/70 (59%)
<b>TUMOR HISTOTYPE</b>	
- Lung cancer:	18
- Nonsmall celi:	15
- Smail celi:	3
- Pancreatic adenocarcinoma:	14
- Colorectal cancer:	13
- Gastric adenocarcinoma:	5
- Biliary tract cancer:	4
- Hepatocarcinoma:	3
- Bladder carcinoma:	3
- Gynecoioic tumors:	4
- Ovarian cancer:	3
- Endometrial adenocarcinoma:	1
- Melanoma:	2
- Soft tissue sarcoma:	4
<b>METASTASIS SITES</b>	
- Soft tissues:	18
- Bone:	2
- Lung:	16
- Liver:	18
- Liver + lung:	6
- Peritoneum:	4
- Brain:	6
PREVIOUS CHEMOTHERAPY:	52/70(74%)

## Results

The clinical response achieved in our patients is reported in Table 2. A complete response (CR) was obtained in 2/70 (3%) patients, who were affected the former by gastric cancer and the latter by lung adenocarcinoma. A partial response (PR) was achieved in other 9 patients (colon cancer: 2; melanoma: 2; lung cancer:1; pancreatic cancer:1; endometrial adenocarcinoma:1; biadder cancer:1; biliary tract carcinoma: 1). Then, an objective tumor regression was observed in 11/70 (16%) patients. A stable disease (SD) was found in other 41

patients. Therefore, a disease control (CR + PR + SD) was obtained in 52/70 (74%) patients, whereas the remaining 18 patients (26%) had a progressive disease (PD). A faith score of at least 60 points was found in 51/70 (73%) patients. By considering faith score in relation to the other individuai variables, no significant differences between males and females was observed in the percent of values of at least 60 points (28/37 (76%) vs 22/33 (67%). On the same way, no difference in the percent of high faith score occurred in relation to the three most frequent neoplasms (lung: 12/18 (67%); colon: 9/13 (69%); pancreas: 9/14 (64%)). Moreover, more surprisingly there was no significant difference in the percent of faith score of at least 60 between patients who followed a specific religion and those who had no religion or no defined religion (22/29 (76%) vs 29/41 (71%). Finally, by considering the clinical response in relation to the faith score, the percent of objective tumor regressions (CR+PR) achieved in patients with faith score of 60 or more was significantly higher with respect to that found in patients with values iess than 60(11/51(19%) vs 1/19 (5%),  $P<0.05$ ). On the same way, the percent of DC (CR+ PR+SD) achieved in patients with high faith score was significantly higher than that observed in those with low faith score (44/51(86%) vs 8/19 (42%),  $P<0.01$ ). Table 3 shows the clinical response in relation to the differeni values of faith score. A progressive increase in the percent of DC occurred concomitantly with the increase in faith score values. Finally, the 3-year survival curves observed in our patients are illustrated in Figure 1. The percentage of 3-year survival reached by patients with faith score of at least 60 was significanti higher than that found in patients with low faith score ( $P<0.05$ ).

**Table 2.** Clinical response (WHO criteria) in 70 untreatable cancer patients in relation to their faith score.

CLINICAL RESPONSE +							
Patients	n	CR	PR	CR+PR	SD	DC	PD
Overall patients	70	2 (3%)	9	11 (16%)	41	52 (74%)	18 (26%)
Faith score > 60	51	2	8	10 (19%)*	34	44(86%)**	7 (14%)
Faith score < 60	19	0	1	1(5%)	7	8(42%)	11(58%)

+ CR: complete response; PR: partial response; SD: stable disease; DC (CR + PR + SD): disease control; PD: progressive disease

\*  $P<0.05$  vs low faith score; \*\*  $P<0.01$  vs low faith score

**Table 3.** Clinical response (WHO criteria) in 70 untreatable cancer patients in relation to the different values of faith score.

CLINICAL RESPONSE							
FAITH SCORE (points)	n	CR	PR	CR + PR	SD	DC	PD
20	5	0	0	0	1	1 (20%)	4 (80%)
40	14	0	2	2(14%)	6	8 (57%)	6 (43%)
60	33	0	3	3(9%)	18	21(64%)	12 (36%)
80	15	1	3	4(27%)	9	13 (87%)	2 (13%)
100	3	1	0	1(33%)	2	3 (100%)	0

## Discussion

This study, carried out in a considerable number of untreatable metastatic cancer patients, would suggest that a neuroendocrine approach with endogenous anticancer molecules, such as the antitumor pineal hormones, and natural antitumor plants, may counteract cancer growth also in patients, who had been considered as untreatable according to the standard anticancer treatments. Moreover, the study shows that the efficacy of therapy is higher in cancer patients with a true spiritual faith, at least in the untreatable ones, even though it cannot be excluded that the reduced therapeutic efficacy observed in patients with low faith score may be simply due to an interruption or a discontinuation of therapy. In any case, even though we are only at the beginning of the possibility to understand the psychochemical mechanisms responsible for mediating the influence of the spiritual faith on the clinical course of the neoplastic diseases, the recent advances in PNEI knowledgements have demonstrated the possibility to modulate the immune system, including the anticancer immunity, by acting on its psychoneuroendocrine regulation [2, 16]. Then, in agreement with the PNEI discoveries, showing a stimulatory effect of both pleasure and spiritual sensitivity and an inhibitory one of stress and depression on the anticancer immunity, it is probable that the increased efficacy of cancer therapies with natural antitumor agents and the prolonged survival time achieved in patients with evidence of spiritual faith may mainly be due to an improvement in the potency of the immune reaction against cancer dissemination [17-19]. Moreover, the study would show that the presence of a real spiritual faith is relatively independent from the adhesion to a specific well defined religion, then it would represent an individual variable rather than to depend on external behaviours, such as the religious practices, by confirming the observations of previous authors, who had considered religion and spirituality as different human conditions [3, 4]. In more detail, since the anticancer action of the pineal hormones and of most antitumor plants is due to both antiproliferative and immunomodulating effects [20], at present, according to the PNEI discoveries, it is possible at present to identify two major functional psychoneuroendocrine systems involved in the mediation of the influence of emotions and spirituality on the anticancer immunity, consisting of the former brain opioid system-pituitary adrenal gland, which is related to stress, pain, anxiety and depression and which plays an inhibitory effect on the anticancer immunity by stimulating T regulatory (T reg) and inhibiting T helper-1 (TH1) lymphocyte functions [21], and the latter brain cannabinergic-mirror neuron-pineal gland functional axis, which on the contrary is related to both pleasure perception and spiritual sensitivity, and which enhances the anticancer immunity by stimulating TH1 and inhibiting T reg activities [22-24]. In any case, both systems would be essential for the survival of the biological species, since the opioid system-pituitary-adrenal gland functional axis would play a fundamental role in the adoptive mechanisms to the environmental and social conditions, while at the other side the cannabinergic system-mirror neuron systems-pineal gland axis would be in relation to the both biological and mind evolution, as suggested by the appearance of cannabinoid receptors in a subsequent time with respect to that of the opioid ones [22], as well as by the evidence of the fundamental role of mirror neurons

in the processes of imitation, learning, language, memory and self-consciousness [23] and of the involvement of pineal molecules, such as the beta-carbolines, in mind expansion [25]. If successive studies will confirm the possibility to prolong the survival time and improve the clinical status of metastatic cancer patients, for whom no other standard therapy may be available, by the administration of natural endogenous and exogenous anticancer molecules, the application of the faith score could allow to predict the probability of efficacy of natural treatments themselves, as well as for the commonly used anticancer therapies in relation to the different tumor histotypes and disease extensions.

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