

## **Clinical study work for evaluation of Immunemodulator Canova® in the therapeutics of oncologic patient considered OTP — Out of Therapeutic Possibility**

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### **Summary**

The present study evaluated the therapeutic answer obtained with the use of the Immunemodulator Canova® in patients with cancer and out of therapeutic possibility (OTP), embracing clinical and laboratory aspects. The results evidenced improvement of the general health conditions, increase of lifetime and changes in the laboratorial profile. Suggesting considerable significance of this medicine in the approach of oncologic patients (OTP) and inciting new studies.

**Key Words: Cancer, oncologic patients, out of therapeutic possibility, Immunemodulador Canova®.**

### **Introduction**

The number of patients with cancer is increasing all over the world. Out of 9 million estimated new cases, more than the half are in developing countries and most of these patients have advanced disease when in the moment of the diagnosis. For them — considered out of therapeutic possibility (OTP) —, the only real option of treatment is the relief of pain and the palliative cares. The expectation is that the mortality for cancer continues to increase globally, mainly due to the progressive increase of age of the population and to the tobacco.

The OTP patients for cancer are a great problem of human and social order, in which the professional that treats the disease is confronted with a dramatic picture of suffering and with enormous difficulty to alleviate it.

Inserted in the search of new treatment ways that make possible to increase the dignity conditions in the continuation of the oncologic disease, the present study evaluated, in the clinical field, the therapeutic answer obtained with the use of Immunemodulator Canova® in oncologic patients and OTP. (1, 2, 5)

### **Theoretical foundations**

One of the established needs for the World Organization of Health – WOH in their recommendations for prevention and control of the cancer was the installment of palliative cares to the patients who are out of the specific anti-tumor therapy. That, more than a professional and the own health system's challenge, becomes an imperious need of our system. (1)

The OTP patients' accompaniment for cancer is accomplished by the professionals of Clínicas de Dor e Cuidados Paliativos of Juiz de Fora (MG), together with the assisting oncologist. (3,5,6)

Palliative care is total active care provided to the patient and to his/her families when it is established that the patient no longer will benefit from the anti-tumor treatment. At this time, the therapeutic focus is on the life quality, the control of the

symptoms of the patient, prolongation of the lifetime and the relief of the human suffering integrated by the trans, multi and interdisciplinary character of the palliative cares.

Of the patients with advanced disease, more than two third feel pain. The control of the algico picture (pain) can be reached through an individualized treatment with the medicine, anesthetic, neurosurgery, psychological and behavior approaches adjusted to the patient's needs who is considered out of therapeutic possibility (FPT) (1)

To increase the possibilities of the professionals' performance involved with the approach of the pain and palliatives cares, other alternatives have been proposed, taking in consideration the natural mechanisms of defense of the host.

In this field, they have been researching new anti-neoplasm drugs and improvement of the prognostic. The growing applications of the biological therapies are the result of a better understanding of the basic mechanisms of anti-tumoral defense. The immunotherapy with T cells has been studied intensely based in the knowledge that those play fundamental role in the control of the tumor growth. (7)

The modifiers of biological answer interfere in this context — MRB, also denominated biomodulators. They are a class of anti-neoplasm agents that present the ability to modify the immune answer to the tumor. An agent can be classified like MRB in case it acts in at least one of the following mechanisms: a) I direct increase of the anti-tumor answer of the host, promoting the increase of the number or of the activity of the effector cells, or still, production of soluble mediators as the citocina; b) reduction of the suppressing mechanisms, promoting the indirect increase of the immune answer of the host to the tumor; c) increase of the defenses of the host through its effect as natural or synthetic mediator of the immune answers; d) modifications of the characteristics of the tumor cells membrane, in way to increase their immunogenicity or to alter their patterns of metastatic dissemination, or, finally, to turn them more susceptible to the destruction for immunology mechanisms and citotoxic agents. (7, 11)

### **Immunemodulator Canova®**

Immunemodulator Canova® is a medicine of homeopathic formulation. The product is characterized by associated dilutions of *Aconitum napellus* + associations, known substances of the Brazilian pharmacopoeia. The combination and the dinamization sequence is essential to reach the final product. It doesn't present toxicity, genotoxicity or identifiable mutagenicity in chromosomal level of human lymphocytes.

This medicine has been used in situations in which the immune system is altered, as in oncologic patient as well as inpatients with HIV. The use of Canova® in patients with several neoplasias seeks to improve all parameters of life quality — decrease of the pain, return of the patient to the social conviviality and improve of the general longer life when compared to the literature.

According to *in vitro* and *in vivo* studies, the medicine is capable to increase the immune answer through functional and structural alterations in macrophages, that start to present structural characteristic of activated cell, as slack cytoplasm, with numerous cellular projections, rich nucleus in euchromatin and substantial increase of the cytoplasm volume; since then, they stimulate the lymphocytes, increasing

their cytolytic power. Besides, with the use of the medicament we verify redistribution of some molecules as integrin alpha and beta-1, actin filaments and receptors Fc, with detection of the activity of the enzyme NADH-oxidize, enzyme that characterizes activated macrophages (State University of Rio de Janeiro). Physiologic alterations are detected in only 48 hours, when the macrophages already show a reduced production of TNF alpha. (PIEMONTE, M. 2000). The decrease of the TNF-alpha (citoxina that provokes caquexia), can be responsible for the patient's best general condition, fact already proved with the use of medicament in vitro. (4, 8, 9, 10, 11, 12)

### **General Objective**

To study the therapeutic action of the Immunemodulator Canova® in oncologic patient and FPT, embracing the improvement of the general condition, life quality, laboratorial follow-up.

### **Specific Objective**

To evaluate the medicament action of Canova®. In the clinical field, through evaluation of detailed physical exam, with prominence for weight, gaining of muscular mass, improvement of appetite, reduction of the symptomology (pain, nauseas and vomits, hiporexia, asthenia, loss of the condition of taking care of oneself) and possible reduction of the dose of the analgesic opioid. In laboratorial level, to evaluate the monthly follow-up of the values of complete blood count, plasmatic pseudocolinesterase, GGT, LDH, TGO, TGP, alkaline phosphatase, total and fractions proteins.

### **Material and methodology**

Canova® was supplied by Canova do Brazil Ltda.

A sample of 26 oncologic patients between 29 and 87 years of age (Picture 02), 11 women = 42,3% and 15 men = 57,7%. Several primary-ranches (Picture 03), in level 4 and out of therapeutic possibility, in other words, patient in quite weakened general health conditions, depressed, important caquexia, frequent complaint of nauseas and vomits.

The whole sample was submitted previously to the suitable conventional treatment for each case: 11 patients are in process with palliative radiotherapy and 4 patient in maintenance chemotherapy (Picture 04), selected and admitted in different dates (Picture 01). Accompanied by the Fundação Amor, philanthropic entity of cancer pain combat, in Juiz de Fora, from March, 2002 to February, 2003, with establishment of treatment protocol with Canova® for 6 months for each patient.

### **Eligibility criteria**

- Confirmation of the cancer diagnosis
- To belong to level 4
- Out of therapeutic possibility, in agreement with the assisting oncologist
- Patient of both sexes
- Previous complementally exams
- To be or not in chemotherapy or radiotherapy treatment

### **Exclusion criteria**

- Jaundice
- Plasmatic cholinesterase inferior to 50% of the reference value between 5000 to 14000 U/l

### **Treatment (9)**

#### **Induction treatment (30 days)**

1. Injectable, 90 flasks of 5 ml, applied 1 flask of 5ml through endovenous way, slow, 3 times a day.
2. Oncologic drops, 4 glasses, being dripped 10 drops under the tongue 4 times a day, far away from the feeding and teeth brushing.
3. Inhalant, 3 glasses, nebulization 3 times a day for 4 minutes, with 3 ml of the medication, without dilution.

#### **Maintenance treatment**

1. Injectable, 16 flasks of 5 ml a month, applied 2 flasks of 5 ml through endovenous way on Mondays and Tuesdays, using insulin needles.
2. Oncologic drops, 4 flasks a month, dripping 10 drops under the tongue, 4 times a day, far from the meals and the teeth brushing.
3. Inhalant, 3 flasks, nebulization 3 times a day for 4 minutes with 3 ml of the medication, without dilution. Only in the cases of compromising lung tumor.

### **Observations**

- All the presentations of Immunomodulator Canova® should be agitated energetically before the administration.
- The inhalant presentation was only used in the cases of compromising lung tumor or of aerial ways.
- Outlying veined catheter Jelco Plus® number 22 was used in most of the cases; the heparinising was made with the solution: dilution of 0,2 ml heparin in 9,8 ml of water double-distilled , applied 0,3 ml of this solution after the application of the medicine.
- In some individualized cases it was used insulin needles for the endovenous application.

### **Evaluation of the therapeutic answer to Canova**

A)

1. Anamnesis, including subjective reports, improvement of the appetite and reduction of the symptomatology (pain, nauseas and vomits, hiporexia, asthenia, loss of the condition of taking care of himself).
2. Detailed physical exam, with prominence for weight and gaining of muscular mass.
3. Evolution through the Karnofsky's Index Acting monthly.

B) Monthly follow-up of the values of complete blood count, plasma cholinesterase, GGT, LDH, TGO, TGP, alkaline phosphatase, total proteins and fractions.

## Observation

Tumor markers and image exams were not requested by Fundação Amor due to poor financial conditions. As the sample was composed of poor patients and OTP (Out of Therapeutic Possibilities), it was difficult to get aid of any hospital or clinic for the image exams and tumor markers.

## Results

It was evidenced in the monthly follow-up a considerable clinic improvement, perceptible mainly in the return evaluation after the thirty days after the beginning of the treatment, where it was already found weight gaining with variable magnitude in 61,5% of the patients (fig. 05), subjective report of improvement by the patient in 85,8% of the sample, improvement of appetite, reduction of nauseas and vomits, increase of willingness for daily activities, no conclusive datum on remission of the algico condition, improvement to the global physical exam with special mention to the coloration of the mucous membranes and the aspect of the skin and phanero. In two patients there was report of hair darkening. Adverse effects were not observed.

In laboratorial level it could be recognized an improvement in the patterns of the blood count in the values related to the anemia and to the common and expected neutropenia in the patients of the sample. Increase was observed in the leukocytes, lymphocytes and monocyte levels. In patients with alteration of the transaminases rates there was tendency, in a variable way, to return to the normality limits. There were two discoveries of significant reduction of the value of PSA. In a case, initial PSA of 57.3 nanog/ml, after the first month of therapy with Canova, was reduced to 1,58 nanog/ml and, the following month, to 0,53 nanog/ml, oscillating close to this value during the evolution. In the second patient, the value of 407 nanog / ml lowered to 19,8 nanog/ml after the first month of treatment; in the third month of the therapy it was 69,8 nanog/ml and it oscillated close to this value in the sequence. These mentioned patients didn't make use of any other therapy for PSA reduction.

During the period of the study, the sample suffered the reduction of 26 to 15 patients, for the following reasons: difficulty of maintenance of vein access in two cases, a case of infection in the totally implanted catheter, precocious death (in the first thirty days of the treatment) of six patients, abandonment of two patients, and one of them obtained important clinical improvement after the first month, besides weight gaining. With relationship to the longer life, the observation allows to infer that there was considerable increase in eight cases, in agreement with the expected literature, besides less expressive increase in other five cases.

For evaluation of improvement of life quality, present in the patient's and family reports, the evolution was used through the Karnofsky's Acting Index, confirming a good clinical evolution. Each case was documented until a relative stabilization or until a period that the general health conditions worsened again and ended up with death. It could be confirmed through the Karnofsky's Acting Index a overcoming of the expectations in relation to the studied patients' expected evolution.

After the end of the treatment protocol (6 months), due to the degree of clinical stability maintained by five patients, it was requested by Canova do Brasil Ltda an extra remittance of medicine for continuity of their treatment. There are still three patients accomplishing the time esteemed by the protocol, however, after four months, it was judged to be enough time for result analysis.

### **Conclusion**

The present study evidenced in the clinical field Immunomodulator Canova therapeutic effectiveness in oncologic patients and Out of Therapeutic Possibilities. The medicine showed to be a weapon of quite useful use in the institution of the palliative cares, for its actions, observed in this study, in relation to the significant improvement of the general health conditions, gaining of weight, reduction of nauseas and vomits, decrease of asthenia and increase of the patients' willingness due to the new vitality observed from the moment that the patients themselves noticed their clinical improvement, besides the adverse effects have not been evidenced.

New studies should be accomplished for deep investigation, statistics and better understanding of these presented clinical results, as well as about the possible action in the reduction of the value of the tumor markers. Thus, while we are completely waiting for an effective anti-neoplasm medicine, we will be able to at least increase the dignity conditions in the continuation of the oncologic disease.

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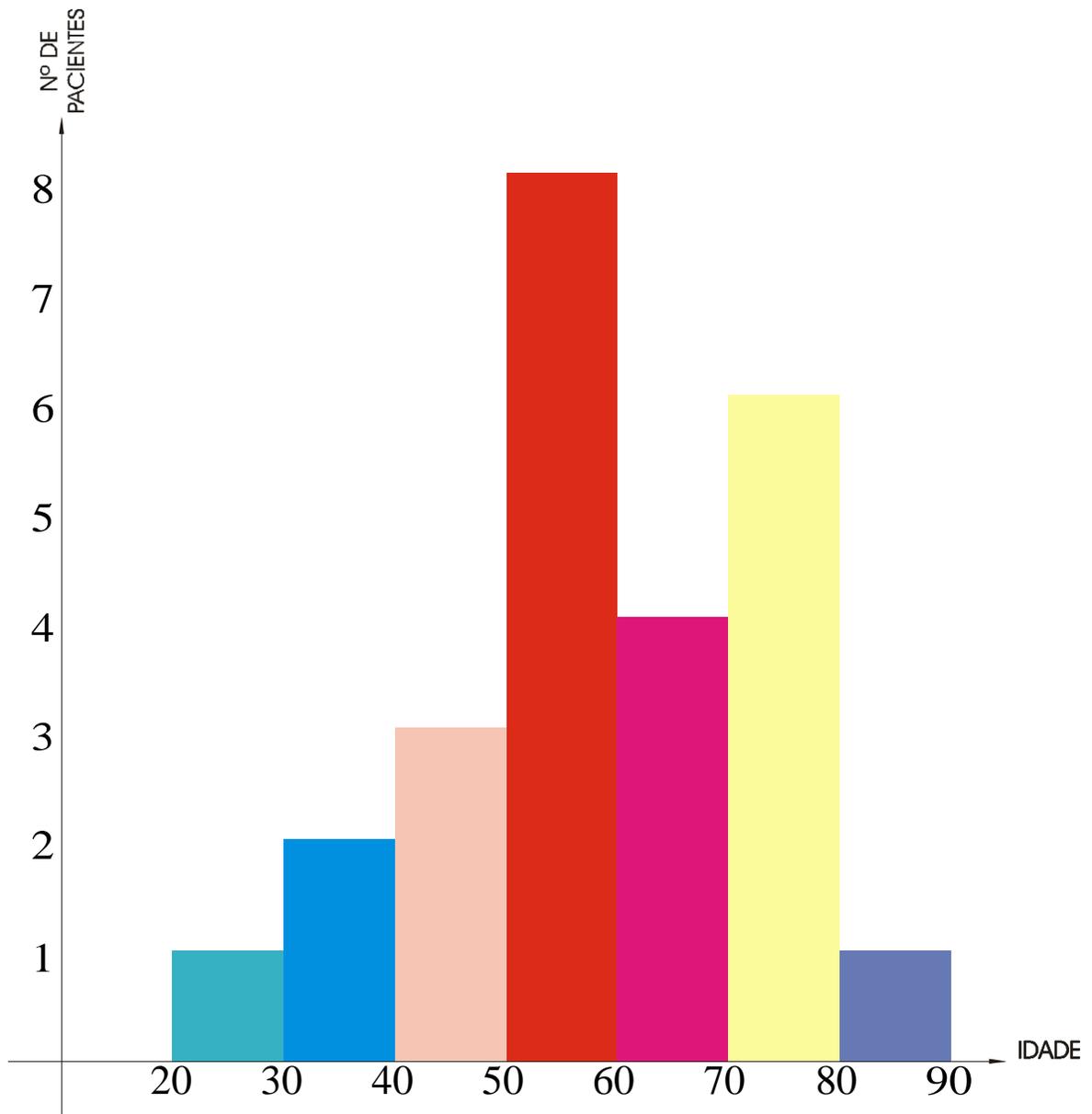
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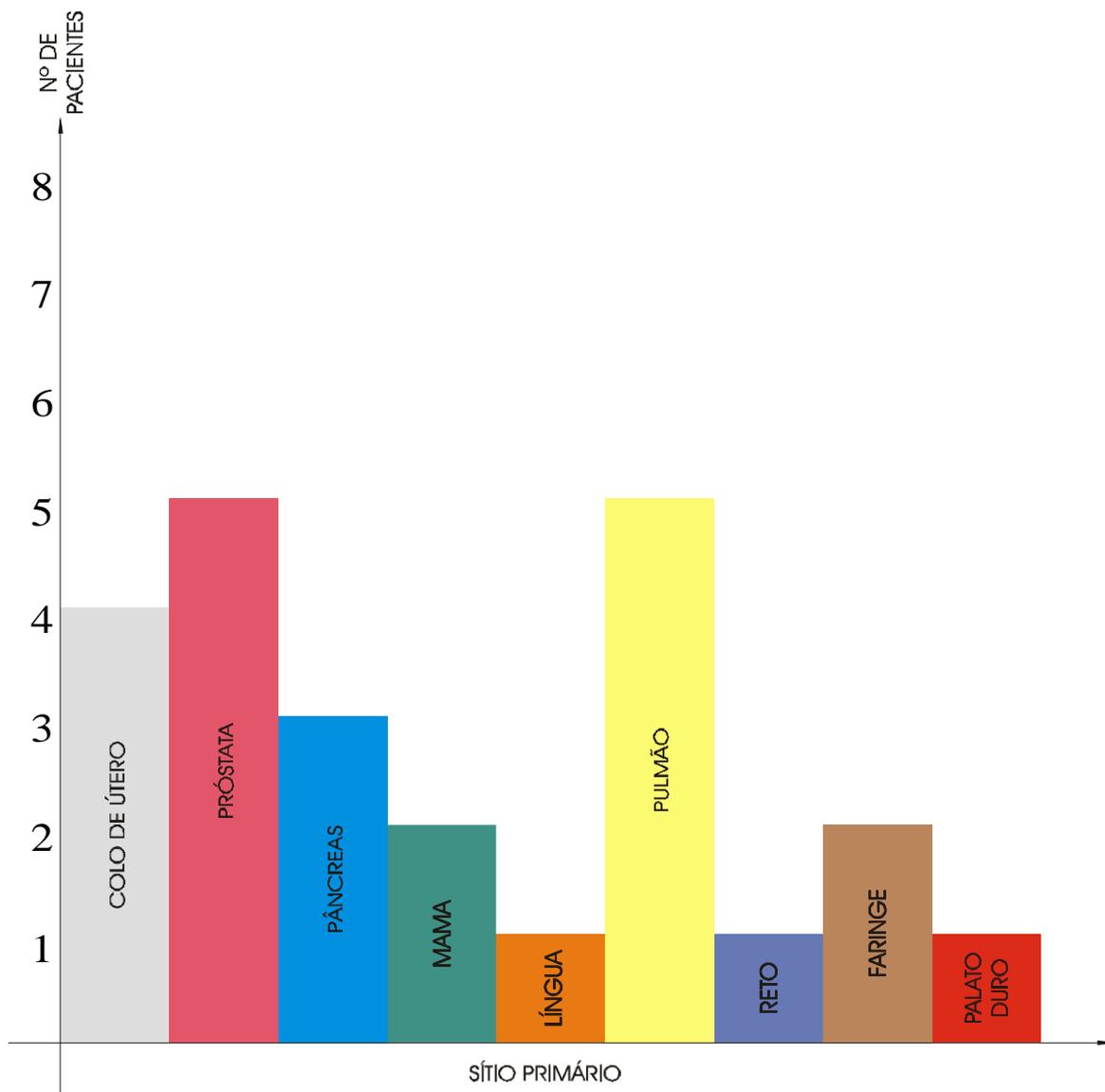
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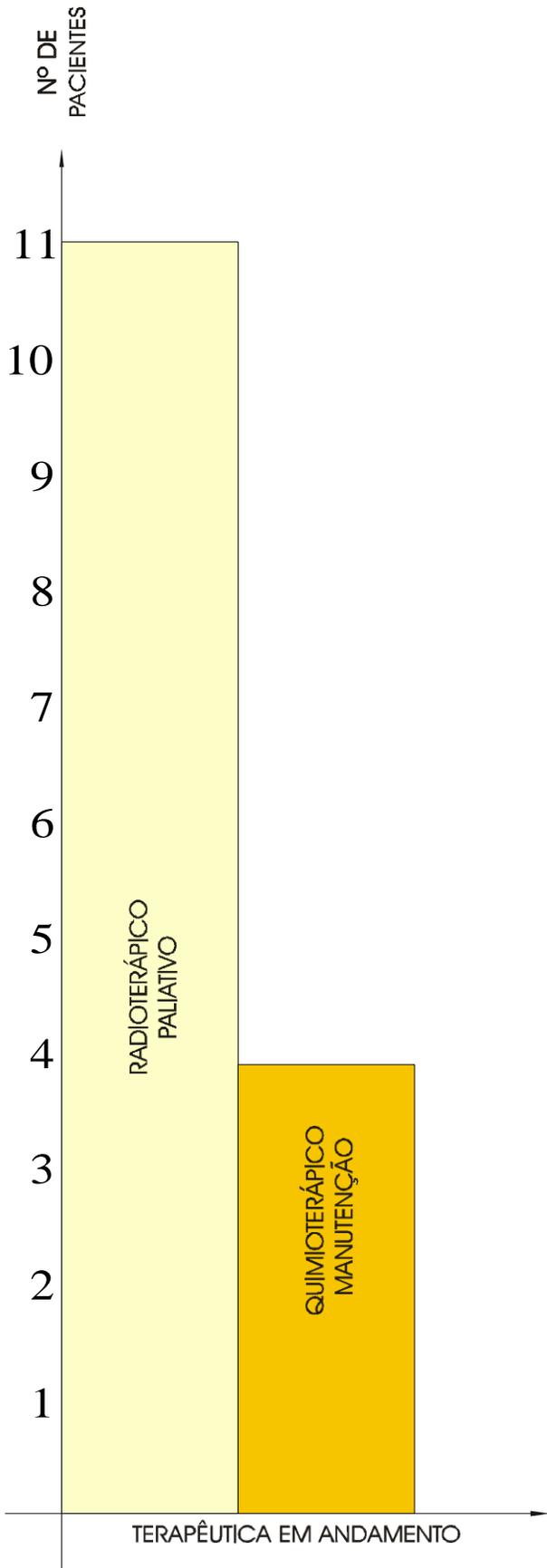
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## VARIAÇÃO DE PESO CORPORAL

	PESO		
	GANHO	PERDA	INCONCLUSIVO
Nº DE PACIENTES	16	2	8
%	61,5	7,6	

Fig. 05

