The Di Bella Method (DBM) improved survival, objective response and performance status in a retrospective observational clinical study on 23 tumours of the head and neck

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Abstract

In 23 cases of carcinoma of the head and neck, the combined use of Somatostatin and/or its analogue Octreotide, prolactin inhibitors, Melatonin, Retinoids, Vitamin E, Vitamin D3, Vitamin C, Calcium, chondroitin-sulphate, and minimal oral doses of cyclophosphamide (50–100 mg/day) led to a decided increase in survival with respect to the median values reported in the literature for the same tumours and stages, together with an evident improvement in the quality of life, partial or complete objective responses and, in some cases, complete and stable cure with functional recovery. The rationale and the mechanisms of molecular biology of the treatment are discussed, showing that the treatment has a differentiating, apoptotic, antiproliferative, antiangiogenic and antimetastatic effect, and, unlike chemo- and/or radiotherapy, preserves and enhances the trophism and functionality of organs, tissues and immunitary and antitumoral homeostasis. This result, achieved without toxicity, demonstrates the efficacy of this biological multitherapy (Prof. Luigi Di Bella’s method or DBM) and is in agreement with the positive results already published on the use of the DBM in various neoplastic diseases. We believe it is of use to report these cases to invite greater interest in the possibilities opened up by this biological multitherapy.

Abbreviations:

ATRA - All-Trans Retinoic Acid
CCK - Cholecystokinin
DBM - Di Bella Method
NOSe - Endothelial Nitric Oxide Synthase
EGF - Epidermal Growth Factor
EGFR - Epidermal Growth Factor Receptor
FGF - Fibroblastic Growth Factor
G - Gastrin
CM - GH-induced monocyte chemotaxis
GF - Growth Factor
GH - Growth Hormone
INTRODUCTION

We present 23 cases of tumours of the head and neck which with DBM achieved a decidedly more favourable ratio between toxicity and therapeutic response compared to conventional treatments. The degree of toxicity was always low, and in any case transitory and easy to treat. In terms of survival, performance status, and objective responses an evident improvement was achieved with respect to the usual therapeutic protocols foreseen for these forms of tumour. The components of the DBM biological treatment and the responses to the DBM treatment are reported.

The rationale of the DBM is briefly described, documenting, with reference to the literature, its scientific basis and pointing out the molecular biology mechanisms of action, the clinical response and the favourable toxicology profile. The diseases treated are all part of the ORL field, even though they differ in histological and immunohistochemical characteristics. Thanks to the constantly better responses compared to the usual treatments, this difference shows the ability of the DBM to effectively interact on the common denominators of cancer: the aimless and uncontrolled proliferation and the mutagenic ability of the neoplastic phenotype. The greatest efficacy and response rapidity was observed in cases treated in the initial stage of the disease and not treated with chemo- or radiotherapy, in which the DBM was applied as first line therapy.

TUMOURS OF THE HEAD AND NECK

In the ORL field, no great differences have been observed in the clinical response to mono or multi-chemotherapy (Casciato et al. 2004; De Vita et al. 1993) that can even temporarily reduce the volume of tumours, the response lasting even less than 2 months. The various cytotoxic and cytolitic protocols, penalised by their high level of toxicity, have not shown any ability to eradicate tumours nor to increase survival (Hashimoto et al. 2003; Jacobs et al. 1990; Ensley et al. 1986; Rooney et al. 1985). Not even monoclonal antibodies, which act on tyrosine kinase proteins and/or on epidermal growth factor receptors (EGFR) or vascular endothelial growth factors (VEGFR), have allowed any considerable increase in life expectancy, merely marginal improvements limited to between a few weeks and 4 months, and in any case penalised by potentially high toxicity. The best result in terms of life expectancy is probably the outcome achieved by the addition of bevacizumab or other monoclonal antibodies to chemotherapy, extending mean general survival by 4 to 5 months. Lapatinib inhibits the tyrosine kinase components of the ErbB1 and ErbB2 receptors, often overexpressed also in tumours of the head and neck, but like the other monoclonal antibodies it is unable to significantly increase survival, nor the disease-free interval. In a recent clinical study with a control group, Lapatinib associated with Capecitabine increased the progression time to 36.9 weeks, with respect to the 19.7 weeks in the group receiving only Capecitabine ($p=0.0032$), confirming the above-mentioned limits.

In tumours of the head and neck, post-operative adjuvant chemotherapy has no effect on disease-free or overall survival (Khafif et al 1991; Jacobs et al. 1990). The correct sequence of radiotherapy – surgery – chemotherapy has not yet been defined due to the absence of statistically documented benefits of chemotherapy (Million et al. 1994; Perez et al. 1992). The advantages of combining chemotherapy with radiotherapy are still under assessment, and while on one hand it seems that the percentage of objective responses can be improved, on the other hand this result is penalised by the high degree of morbidity and the decline in quality of life without any increase in terms of mean values of survival (Hashimoto et al. 2003; Vokes et al. 1994; Khafif et al. 1993; Laramore et al 1992; Perez et al. 1992).

CASE SERIES

1. Cancer of the larynx ($T_1N_0M_0$), squamous cell infiltrating tumour involving the anterior 2/3 of the left vocal cord, as far as approx. 1 mm from the anterior commissure. Complete regression and functional recovery after little more than a year's treatment with DBM. Discontinuation of the treatment for 14 months after hospitalisation for vascular problems and hyperglycemia seizures. Approx. 2 years after discontinuing DBM, recurrence with involvement of the anterior commissure, subcordal and contralateral extension, fixing of left vocal cord, absence of satellite adenopathies and metastases ($T_3N_0M_0$). Resumption of DBM associated with radiation therapy, in complete remission for the last ten years.

2. Carcinoma of the larynx ($T_3N_1M_0$): vegetative growth of the laryngeal face of the epiglottis, extending to the vocal cords with limitation of mobility. Over 50% regression after six months of treatment.
3. *Carcinoma of the larynx (T2N1M0): infiltrating supraglottic tumour, extending to the vocal cords, bilateral anterior commissure with cordal fixity, refused laryngectomy, DBM associated with radiotherapy. Complete response, disease-free for approx. nine years, decease due to vascular problems.

4. *Medullary carcinoma of the thyroid (T3N3M1), with disseminated pulmonary lymph node repetitions, critical and severely declining conditions at the start of DBM, objective response of approx. 50% after 14 months, with evident recovery of performance status.

5. *Papillary carcinoma of the thyroid (T3N3M1) with multiple pulmonary and bone repetitions. More than 1 year after starting DBM, stability of the disease with evident improvement in quality of life.

6. *Papillary carcinoma of the thyroid (T3N1M1), after surgery and treatment with radio-iodine, radiotherapy and chemotherapy, mediastinal lymph node, disseminated bilateral pulmonary and pharyngeal progression, with extension to the surrounding muscles, dysphagia due to esophageal compression. The patient underwent tracheotomy, was discharged with pain therapy in August 2003, in September started DBM with regression of almost 50%, good quality of life, resolution of the dysphagia. Treatment continued until October 2008, deceased due to meningitis, followed by pneumonia.

7. *Squamous cell carcinoma of the right tonsil (T1,N0,M0), no adenopathies or metastases, not operated on, treated only with DBM, objective response over 50%, stable for over a year. Good quality of life.

8. Carcinoma of the right tonsil, poorly differentiated (T1,N0,M0), treated with neoadjuvant DBM, operated on, no surgical latero-cervical removal of lymph nodes, subsequent adjuvant application of DBM. No adenopathies or metastases, disease-free for 10 years.

9. Sarcoma of the right maxillary sinus (T3N1M0), extending inferiorly to the alveolar and palatine bones. Neoadjuvant application of DBM. Non-radical surgery, treated with adjuvant DBM, in remission from 1996 to 2005, widespread recurrence at the end of 2006 (approx. 2 years after completely stopping DBM despite the indications for reduced dose maintenance). Surgery in 2007 and restart of DBM, no metastases, signs of slight local progression. Deceased approx. 1 year ago during revision surgery.

10. *Squamous cell carcinoma of the esophagus (T2N0M0) localised in the middle 3rd. After 3 months of treatment with DBM improvement in quality of life, progression blocked with stability and recovery of ability to swallow.

11. *Squamous cell carcinoma of the esophagus (T2N0M0) with poor cervical differentiation, no previous treatment. Evident endoscopic, radiological, subjective and clinical improvement after 10 months treatment, with recovery of ability to swallow and good performance status.

12. Carcinoma of the esophagus (T3N1M1), poorly differentiated, superficially ulcerated with 360° involvement of the 5 distal centimetres of the esophagus close to the cardia ventriculi, unoperable. The patient underwent combined chemo-radiotherapy with objective response of approx. 50%. Treatment was stopped due to severe hemorrhagic complications and multiple transfusions were performed. The patient was discharged in June 1995 in very poor conditions with palliative and pain therapy at home. In August 1995 progression of the disease, in September 1995 start of DBM. The patient is alive and continuing DBM with reduced maintenance doses; disease-free.

13. Vegetating carcinoma of the rhinopharynx (T3N2M0), poorly differentiated with partial rhinostenosis and homolateral tubal stenosis. Operated on in 1975 with bilateral and laterocervical removal of the lymph nodes according to Suarez, localised rhinopharyngeal radiotherapy, treated with DBM (without somatostatin), in remission for 33 years. Currently receiving small doses of MLT and retinoids as maintenance therapy.

14. *Adenocystic carcinoma (T1,N0,M0) of the left parotid gland, homolateral, laterocervical and pulmonary metastases, widespread involvement of the facial mass. After little more than a year’s treatment with DBM, pulmonary and facial regression of 50%. Good quality of life.

15. Carcinoma of the rhinopharynx (T3N2M0) with flat epithelium, highly undifferentiated and extending from the left tubal border stenosed to the choana and beyond the mid line of the vault of the rhinopharynx. Metastases in 2 homolateral subjugulo-digastric lymph nodes and one in the contralateral spinal chain. Operated on in 1976 with laterocervical and bilateral removal of the lymph nodes according to Suarez, localised rhinopharyngeal radiotherapy, treated with DBM (without somatostatin), in remission for 32 years. Currently receiving small doses of MLT and retinoids as maintenance therapy.

16. Carcinoma of the tongue and floor of the mouth (T2N1M0) infiltrating, ulcerative with lesions of the tongue and floor of the mouth. Not operated on, treated with DBM before, during and after radiotherapy. In remission for 14 years.

17. *Ulcerated carcinoma of the right tonsil, with extracapsular extension to satellite adenopathy (T3N1M0). Started neoadjuvant DBM and immediately after surgery, after less than 1 year reduced the doses continuing with 10 mg of MLT and a spoon-
ful of retinoids and Vit D3 as maintenance therapy. In remission for 11 years.

18. Carcinoma of the left parotid gland, NAS-G3 (T2N1M1), operated on at the age of 11 years for cylindroma of the left parotid and treated with radiotherapy. Recurrence at the age of 34 years (2004), radical parotidectomy with homolateral laterocervical removal of the lymph nodes at the 3rd level, followed by chemo-radiotherapy. A few months later, progression extending throughout the pterygoid compartment and posteriorly to the ramus of the mandible with functional block of the temporomandibular joint. Disseminated pulmonary mantle progression of the lower right lobe and a 1.7 cm postero-basal nodule in the upper right lobe were also detected. Sub-continuous and intense pain, accentuated by mastication which was extremely difficult. After a few months a chest CT scan showed widespread and massive bilateral pulmonary progression. Started DBM in October 2005 with progressive reduction of the functional damage and pain, and return to work. Instrumental tests showed a subtotal objective response at the site of the primary lesion and over 50% at pulmonary level. A subsequent chest CAT scan showed the persistence of of residual bilateral pulmonary nodules, but the various CT-PET scans did not show any absorption of the radio-compound due to the lack of proliferative activity of the lesions. The patient is continuing the DBM with good performance status and is still working.

19. Squamous cell carcinoma of the tonsil G2 (T3N2M0). In September 2008, a large, solid and expansive neoformation was detected in the right tonsillar pillar, 3.7 cm along its main axis and extending 7 cm craniocaudally, occupying 3/4 of the oropharynx, with some 2 cm lymph nodes in the cervical homolateral position and other larger ones along the contralateral nervo-vascular axis and in the rear neck triangle on both sides. Surgery was not performed as the patient suffers from post-ischemic dilatory heart disease. The patient started biological DBM in the following month and simultaneously underwent radiation treatment for approx. 30 days. Still following DBM, having achieved complete remission and good quality of life.

20. *Squamous cell maxillary carcinoma (T3N2M0).* 90-year-old patient in whom in May 2010 a lesion was detected which almost completely obliterated the maxillary sinus with complete bone destruction of the floor and of the posterior and lateral wall. Right latero-cervical lymph nodes increased in size (13 mm). Due to the extent of the tumoral mass and the patient's age, no conventional surgical or pharmacological treatment was prescribed and the patient followed only biological DBM therapy. Improvement in quality of life and progression blocked. Stable.

21. Basal cell carcinoma of the lips, extensively infiltrating the muscle planes, with perineural carcinoma (T1N0M0). In May 2008 the patient underwent exeresis and again in June due to widening of the resection margins which were focally involved. In August of the same year, the patient started DBM treatment. Currently in complete remission.

22. Tympano-jugular paraganglioma treated surgically in 1987 with subsequent (2004) bilateral local recurrence (max. 8 cm) associated at mediastinic level with 9 cm lesion. Right hemiparesis. Under treatment with DBM since 2006 and it is currently possible to confirm the stability with complete block of progression. Modest quality of life.

23. Squamous cell infiltrating carcinoma (T4N3M0) localised in the epiglottis and hypopharynx, with latero-cervical and supraclavicular lymph node involvement, diagnosed in 1997. The patient, a well-known actor, refused surgery so as not to compromise his career, and started first-line DBM treatment associated with radiotherapy. In complete remission until death due to other causes 6 years later.

* Cases which have applied to an Italian court to receive DBM free of charge, undergoing assessment by a panel of 3 medical consultants, and on the basis of a merit score, have obtained DBM treatment free of charge. The decisions are based on data documenting the objective response, and clear improvement in the quality of life with DBM.

**DRUGS INCLUDED IN THE DBM**

1. **All-trans retinoic acid**
   - Axeroftol palmitate
   - Betacarotene
   - Alpha-tocopheryl acetate

   These molecules are mixed in solution form, a formulation which allows maximum bioavailability, in these ratios:
   - All-trans retinoic acid 0.5 g
   - Axeroftol palmitate 0.5 g
   - Betacarotene 2 g
   - Alpha-tocopheryl acetate 1000 g

   The daily dose is calculated on the basis of body weight decimals: a 70 kg adult can therefore take 7 g of solution 3 times a day.

2. **Melatonin** tablets, in Prof. Di Bella’s formulation, chemically complexed as follows: Melatonin 12%, Adenosine 51%, Glycine 37%, administered in tablets in doses of 20 to 60 mg per day.

3. **Bromocriptine**, 2.5 mg tablets, one tablet per day, 1/2 tablet morning and evening
4. Cabergoline, 0.5 mg tablets Can be used together with or instead of Bromocriptine, administering 1/2 tablet twice a week

5. Dihydrotachysterol, synthesis Vit. D₃, 10 drops before meals together with the retinoid solution 3 times a day

6. Chondroitin-sulphate, 800 mg sachets, one in the morning and one in the evening diluted in water

7. Cyclophosphamide, 50 mg tablets, one/two a day instead of cyclophosphamide

8. Hydroxyurea, 500 mg tablets, one/two a day instead of cyclophosphamide

9. Somatostatin, peptide of 14 amino acids, 3 mg per day, injected after the evening meal, slowly and subcutaneously or intravenously with a 12-hour timed syringe (evening administration is indispensable as it coincides with the nocturnal peak of GH secretion and GH-dependent growth factors)

10. Octreotide, peptide of 8 amino acids, in 1 mg/die vials, with the same administration method as above (alternatively, the delayed-release formulation of Octreotide can be used intramuscularly at the same doses)

11. Vitamin C, 2–4 g per day, orally

12. Calcium, 2 g per day, orally

CONCLUSIONS

The biological neuro-immuno-endocrine treatment devised by Prof. Luigi Di Bella (DBM) applied in the cases described above acted by means of a receptorial, differentiating, apoptotic, antiproliferative and antiangiogenic mechanism of action which totally differs from the usual cytolytic therapies. Partial or complete objective responses were slowly and gradually achieved, demonstrating a high level of tolerability and a favourable toxicological profile, in addition to a distinctly better therapeutic response in terms of survival, quality of life and objective response with respect to chemotherapy protocols.

DISCUSSION

Rationale of the treatment

An extensive and in-depth study of the medical-scientific data banks clearly shows a serious discrepancy between the scientific data and the oncological protocols. This is due to the lack of value attributed to differentiating and proapoptotic, antiproliferative, antiangiogenic, and anti-metastatic antitumoral molecules with minimal toxicity and high antiblastic potential such as Somatostatin and its analogues, Melatonin, prolactin inhibitors, retinoids, and vitamins D3, E and C. The use of 13 Cis-retinoic acid has been surpassed by the greater tolerability and therapeutic manageability of All Trans retinoic acid (ATRA), its bioavailability, efficacy, tolerability and half-life being enhanced in the DBM by its inclusion in a solution with Vit E and other retinoids (in the above-mentioned proportions of 0.5 g of ATRA, together with 0.5 g of Axerofitol Palmitate and 2 g of Betacarotene in 1000 g of Alpha Tocopheryl Acetate, protecting the retinoids from the high oxidative instability). The regular administration of minimum, apoptotic, non-cytolytic and thus non-mutagenic doses of cyclophosphamide, thanks to its myeloprotective, antidegenerative and trophic action on parenchyma and tissues, of MLT and of high doses of Vitamin E, Retinoids, vitamins C and D₃, and folic acid eliminated in almost all cases the medullary toxicity of continuous administration for apopotic purposes of 50–100 mg per day of Cyclophosphamide, allowing a gradual recovery and maintenance of good performance status. (Pacini et al. 2011; Di Bella 2010; Di Bella et al. 1979; 2006). In the use of the DBM, only in a small percentage of cases previously undergoing massive doses of chemotherapeutic agents, the dose of cyclophosphamide to 50 mg and to use erythrocyte and granulocyte growth factors. This does not compromise the effect of the cure but merely delays the apoptotic response to which all the other components of the DBM contribute synergically and factorially. Loss of differentiation and proliferation are common denominators of all tumours, albeit to different extents. The ubiquitary receptorial expression of Prolactin (Ben-Jonathan et al. 2002; Hoogh et al. 1998;) and of GH (Lincoln et al. 1998; De Souza et al. 1974) represent one of the aspects of the direct and generalized mitogenic role of these molecules.

Cellular proliferation is closely dependent on Prolactin, GH, the main growth factor, and on the GH-dependent mitogenic molecules which it positively regulates, such as EGF, FGF, HGF, IGF1-2, KGF, NGF, PDGF, VEGF and TGF, as well as on growth factors produced by the gastrointestinal system, such as VIP, Cholecystokinin, Gastrin, and probably on P substance.

Both physiological and tumour cell proliferation are triggered by the same molecules, used by the tumour cells to an exponential extent with respect to the healthy cells. Biological antidotes of GH, such as Somatostatin and its analogues, not only reduce the expression and transcription of highly mitogenic growth factors, such as IGF1-2 (Schally et al. 2003; Cashinu et al. 2001; Shally et al. 2001), EGF (Held-Feindt et al. 1999), and FGF (Mentlein et al. 2001), but extend their negative regulatory action to the respective receptors with evidences of antiproliferative and antiangiogenic effects (Bocci et al. 2007; Florio et al. 2003; Albini et al. 1999; Szepesházi et al. 1999; Barrie et al. 1993).
It is known that the GH-IGF1 axis has a determining effect on the biological development of a tumour. The IGFRs respond mitogenically to IGF. The suppressing effect of SST and its analogues on the serum levels of IGF1 is both direct, through inhibition of the IGF gene, and indirect, through suppression of the GH and thus of its hepatic induction of IGF1. Essential phases of angiogenesis (the main stage of tumour progression), such as GH-induced monocyte chemotaxis, interleukin 8, endothelial Nitric Oxide Synthase, Prostaglandin E2 and growth factors that are essential and synergic for the development of angiogenesis, such as VEGF, TGF, IGF1, FGF, HGF and PDGF, are all negatively regulated by Somatostatin and its analogues (Arena et al. 1997; Sall et al. 2004; Florio et al. 2003; Jia et al. 2003; Cashin et al. 2001; Watson et al. 2001; Turner et al. 2000; Vidal et al. 2000; Albini et al. 1999; Barrie et al. 1993; Wiedermann et al. 1993). The inhibition of angiogenesis, induced by SST, is synergically reinforced by the other components of the DBM, such as MLT (Di Bella 2010; Di Bella et al. 1979; 2006; Lissoni et al. 2001), Retinoids (McMillan et al. 1999; Majewski et al. 1994; Hasson et al. 1990;), vitamin D3 (Kisker et al. 2003; Mantell et al. 2000), Vitamin E (Neuzil et al. 2001; Tang et al. 2001; Shklar et al. 1996) Vitamin C (Ashino et al. 2003), prolactin inhibitors (Turner et al. 2000), and components of the extracellular matrix (Liu et al. 2005; Ozerdem et al. 2004). The components of the DBM also extend their synergetic action to the amplification of the cytokine, antiproliferative and antimetastatic effects of Somatostatin:

MLT (Kumar 2004; Cos et al. 2000; Mediavilla et al. 1999; Maestroni et al. 1996; Kvetoň et al. 1986)
Vit. D3 (Jensen et al. 2001; Barroga et al. 2000)
Cabergoline and Bromocriptine (Ben-Jonathan et al. 2002; Gruszka et al. 2001)
Chondroitin-sulphate, components of the extracellular matrix (Pumphrey et al. 2002; Batra et al. 1997)

A causal relationship has been demonstrated between the receptorial expression of GH and tumour induction and progression, by histochemically detecting much higher concentrations of GHR in the tumour tissues compared to physiological tissues, and by showing the potent mitogenic role of GH with a dose-dependent proliferative index (Lincoln et al. 1998). This role is both direct, i.e. receptorial, and indirect, through GH-dependent (Friend 2000) induction of the hepatic expression of IGF1 and of the other GF. We believe it is worth insisting on the determining role of the GH-IGF1 axis in the biological behaviour of many tumours. (Hagemeister et al. 2008; Murray et al. 2004). IGF1 receptors which respond mitogenically to the ligand have been identified in an extremely high and subto- tal percentage of various neoplastic cells. Somatostatin exerts its antiblastic activity both directly on the tumour cells (Lee et al. 2008), and indirectly, by suppressing the GH, on which the secretion of IGF1 depends as well as by inhibiting the expression of the IGF1 gene (Hagemeister 2008; Durand et al. 2008; Florio 2008; Murray et al. 2004; Sall et al. 2004; Barnett et al. 2003; Schally et al. 2001; 2003).

Several studies have also been published on the inhibitory activity of SST on another powerful mitogenic growth factor, EGF, through a number of mechanisms:

- dose-dependent inhibition of the tyrosine phosphorylation induced by the activation of EGF by SST (Durand et al. 2008; Lee et al. 2008; Mishima et al. 1999; Pawlikowski et al. 1998)
- reduction of EGFR in the tumour cells (Szepésházi et al. 1999);
- reduction of the expression of EGF (Held-Feindt et al. 1999);
- suppression of the plasma concentration of EGF (Cashin et al. 2001).

Mitogens produced by the gastrointestinal system, such as VIP, CCK and G, are strongly inhibited by somatostatin and/or octreotide (Kath et al. 2000), the efficacy of which is reinforced through a synergic factorial mechanism with the other components of the DBM. The literature has therefore confirmed the anti-neoplastic, differentiating and antiproliferative, antiangiogenic and antimetastatic mechanisms of action of all the components of the DBM.

The DBM biological treatment led to a net improvement in performance status, and, with respect to chemotherapy, at all stages it increased the mean survival values reported in the literature in the same tumours and stages. This is confirmed by the results published in Cancer Biotherapy, regarding the application of the DBM in stage 3 and 4 non-small-cell lung cancer (Norsa et al. 2006; 2007), in low-grade non-Hodgkin’s lymphoma (with the worst prognosis) (Todisco et al. 2001) and in breast cancer (Di Bella 2008; 2010).

As the DBM is a biological treatment, it does not, unlike cytotoxic therapy, achieve rapid decreases in volume; instead it leads to slow and gradual objective responses by activating the above-mentioned receptorial targets, without any significant toxicity. Unlike chemotherapy, it does not induce but inhibits changes, oxidative reactions, and the increase of free radicals or immunatory depression, also enhancing the trophism and functionality of epithelia, endothelia, parenchyma and tissues of the extracellular matrix, triggering antiblastic homeostasis and the biological conditions that allow physiological life to prevail over neoplastic biology. It is, therefore, reasonable to suggest that early application of this method as the first-line therapy in...
a patient who has not been debilitated by the toxic, mutagenic and immunodepressive effects of chemotherapeutic or radiotherapy could achieve decidedly better results. We believe it is useful to report these cases in order to invite a greater interest and more in-depth studies on the possibilities opened up in oncology by the immunonuroendocrine, biological and receptorial treatment of the DBM.

REFERENCES


