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Predictors of long-term survival in stage IV malignant melanoma (MM) patients

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A small proportion of patients (pts) with stage IV MM has long survival. In order to provide pts with more meaningful prognostic information, we have analysed the variable "long-term survival", defined as survival for at least 2 years after the date of first metastasis. A cohort of 13 long term survivors (LTS) has been identified among 86 pts with stage IV disease during the period 1986–1996. The control group (C) consisted of 73 pts who have survived for less than 2 years. 11 factors have been analysed. For the LTS the median age was 58 y. 62% were females. The primary site was in extremities in 31%, the trunk in 31% and the H/N in 15%. All the pts had presented initially with stage I or II disease. The median disease-free interval (DFI) prior to diagnosis of stage IV disease was 31 m. Lymph node dissection underwent 10/13 (77%) LTS and 2 of them received adjuvant chemotherapy. None of these characteristics differed significantly between LTS and C group. However, 6/13 (46%) LTS achieved a PR to the first therapy compared to only 12/73 (16%) (P = 0.01). In conclusion, the response to front line therapy (chemo and/or immunotherapy) for the metastatic disease has been identified as the most important prognostic variable in our study.

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Photodynamic therapy (PDT) and photodynamic detection (PDD) in melanoma

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Purpose: Photodynamic therapy (PDT) involves the action of light on a photosensitizer (usually porphyrin) retained in malignant tissues. High level of porphyrins is noticed in melanoma tissue, therefore photodynamic treatment of melanoma is hopeful. There is on experience on excellent results of choroidal melanoma's (PDT), but a large number of scientists certify that the results of skin melanoma's PDT are poor. This work is aimed to new specific PDT method proposed by us required for skin melanoma.

Methods: usually photosensitizes is injected and 24–48 h later melanoma like other tumour is irradiated with 200–300 mw red light. At the beginning of such irradiation the superficial necrotic armour appears and through it light penetration to a deeper tissues of melanoma becomes difficult. The total of 48 patients (89 tumours) have been treated by us with the new PDT method. On the first day, after i/v injection of a photosensitizer melanoma was irradiated with a low power red light (30–50 mw) from Helium-Neon laser. After that, when the first changes in malignancy begin we irradiated the tumour with Gold vapour laser 75–100 mw power red light. The absorbed light energy was 200 J/cm^2. The third day tumour was irradiated with 200 mw power red light. Cytological studies of tumour tissues were performed for each malignant focus until PDT. Histological examination was provided only once, on the 5th–10th day after PDT, after a wide excision of the melanoma. There were also a control group 51 patients with primary cutaneous melanoma (T_{1-4} N_0M_0) treated by us.

Results: Full necrosis of 73 malignancies in 35 patients, significant necrosis of 9 melanoma's in 7 patients, partial necrosis of 4 tumours in 3 patients and no evidence of necrosis of 3 tumours in 3 patients was the immediate results of PDT. In some cases of histological examination together with tumours necrotic tissues, a healthy mole's tissue was found. This phenomenon was used for PDD in patients with multiplex skin melanoma. All patients were followed up for the period from 10 to 78 months. Among 30 patients (20%) in 3 of them (10%) it caused death.

Conclusions: 1. Photodynamic skin melanoma's treatment, due to morphological and biochemical properties of melanoma's tissue, requires a special PDT method.

2. Adequate pfotodynamic therapy is a really effective method in primary skin melanoma's treatment in all the cases when it is possible.

3. According to our observation, PDT is effective when treating local melanoma's recurrences, too.

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Soluble tumor markers in malignant melanoma. A quantitative analysis of S-100, of CD44 and of its variant isoforms

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Molecules expressed on tumor cells may be released in the serum and provide useful markers for assessing tumor bulk, disease progression, response to therapy as well as yielding prognostic factors. Tumor cell markers have been used for diagnostic purposes in melanoma with contrasting results. Expression of the S-100 protein is commonly evaluated by immunohistochemical techniques that do not lend themselves to precise quantitation. CD44 standard (st) is an adhesion molecule expressed on normal and neoplastic cells and in some solid tumors. In some cancers, expression of certain CD44 variants, such as V5 and V6 associate with high metastatic potential. In this study, we have measured S-100, using an IRMA assay (Byk Gulden, Milano, Italy), and CD44 st, V5 and V6 isoforms using an ELISA assay (Bender MedSystem, Vienna, Austria) in the serum of 79 normal subjects and 128 melanoma patients (pts). Using the three stage classification system pts were at stage I (67), II (35) and III (26). The cut-off levels determined in controls were 0.13 mg/ml for S-100, 595.2 ng/ml for CD44 st, 57.6 ng/ml for CD44 V5 and 248.5 ng/ml for CD44 V6. The amount of S-100 in the serum was significantly related to tumor stage, since we found serum levels above the cut-off threshold, in 9%, 14% and 50% of the patients at stage I, II and III respectively. Much lower percentages of melanoma pts were positive for CD44 st, V5 and V6 at each disease stage, and percentages of pts with CD44 above the threshold level never reached 20%. At variance with what is shown in other cancers (lung, ovary, stomach, colon), CD44 monitoring in melanoma does not seem to provide a sensitive marker in evaluating the extension of the disease while preliminary follow-up studies, in a limited number of pts, suggest that CD44 serum levels may provide a useful indicator of disease progression.

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True hyperthermic antiblastic limb perfusion for stage I melanoma: An appraisal of survival gain

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Introduction: The role of prophylactic isolated limb perfusion for high risk melanoma in stage I is currently under investigation. A randomized study in mild hyperthermic (38°C) conditions has failed to give clear results on the role of perfusion as adjuvant treatment. We strongly believe that a "true" hyperthermic regimen (41.5°C) in strictly temperature-controlled conditions may give further definitive indications.

Patients and Methods: In our Institution 29 patients suffering from stage I (M.D. Anderson Hospital scale) lower limb melanoma with Breslow thickness greater than 2 mm, meeting the elegibility criteria, were submitted to isolated limb perfusion in "true" hyperthermic conditions. Male/female ratio was 7:22, mean Breslow thickness was 3.02 mm, mean age 52.5 yrs. A standard dosage of 10 mg/lt of melphalan was administered when all limb temperatures reached 41°C. An hyperthermic phase of 90 minutes followed targeting to 41.5°C throughout the limb. Additional surgical procedures were performed as required. Pharmacokinetic assays for melphalan plasma levels were also carried out.

Results: Mean follow up is 22.9 months. Twenty-three pts are currently alive and disease-free, 1 pts had in-transit metastases, 2 pts had a femoral nodal relapse, 2 pts died of disease and 1 pts for other disease. Systemic and regional toxicity and pharmacokinetic data are comparable to our previous experience with mild hyperthermia treatments.

Conclusion: In our opinion these early results are encouraging, nevertheless further confirmations are needed.

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Dacarbazine and tamoxifen in patients with advanced melanoma: An effective therapy option?

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Purpose: The clinical outcome of patients with advanced metastatic melanoma is still worse and several therapies were acquired to enhance