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POSTER

Standards, options and recommendations: Clinical practice guidelines for diagnosis, treatment and follow-up in cutaneous melanoma (cm)

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Context: The "Standards, Options and Recommendations" (SOR) project is a collaboration between the Federation of the French Cancer Centers and specialists from French public Universities, general hospitals and private clinics. The main objective is the development of clinical practice guidelines to improve the quality of care and outcome for cancer patients. The methodology is based on literature survey and clinical appraisal by a multi-disciplinary group of experts, with feedback from specialists in cancer care delivery.

Objectives: To develop clinical practice guidelines according to the definitions of SOR for the management of cutaneous melanoma.

Methods: Data have been identified by literature search using Medline and Current Contents (Dec. 1998) and the expert personal reference lists. Once the guidelines were defined, the document was submitted for review to national and international independent reviewers and to the medical committees of the 20 Cancer Centers.

Results and Conclusions: The main recommendations for CM management are:

Diagnosis of CM requires a surgical removal of the lesion and its histological examination.

The pathology report must state the presence of melanocytic cells, malignant features, the maximal thickness and the consistency of the surgical margins. If required, a new surgical excision must be performed. No additional treatment, including elective regional node dissection or medical adjuvant treatment, is integral to the standard care at this stage. In case of metastatic regional lymph nodes, a complete lymphadenectomy is required in the absence of other metastases. Adjuvant treatment with high-dose alpha interferon is optional in this case. In advanced disease, palliative treatments only are available and chemotherapy using DTIC represents the reference treatment. The role of sentinel node detection and prophylactic local lymphadenectomy as well as the potential benefit of interferon in adjuvant treatment are important issues for the future management of CM. We recommend to actively pursue clinical trials in this setting. Follow-up is based on physical exam and self-detection must be encouraged during the patient life. Medical follow-up for early diagnosis is also recommended in high-risk groups.

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PUBLICATION

Cost-effectiveness of interferon for high-risk (stage III) melanoma patients

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Objective: To determine the cost-effectiveness (C/E) relationship of adjuvant high-dose interferon alfa-2b (IFN) treatment vs. observation in patients with surgically resected stage III melanoma (AJCC).

Methods: Disease progression was studied using a Markov model (B.E. Hillner, *J Clin Oncol* 1997; 15: 2351-2358), according to the results of ECOG1684 (J.M. Kirkwood, *J Clin Oncol* 1996; 14: 7-17). The cost of each clinical state from the Health Authorities perspective was determined by an expert panel, according to routine clinical practice in Spain.

Results: For a patient with a mean age of 50 years, lifetime incremental cost (IC) with a 6% discount rate, life years saved (LYS) and incremental C/E relationship (6% discount cost per LYS) are shown below:

Cost (in euros) IC LYS IC/LYS
IFN vs. Control 17666 1.9 9015

According to the projection generated by the model, IFN treatment produces an increased survival of 1.9 years with an incremental cost per LYS of 9015 euros. This result was compared with essential procedures for survival which are accepted by our National Health System (NHS), such as hemodialysis for patients with renal failure (20194 euros/year).

Conclusion: IFN administration in high-risk (stage III) melanoma, a disease in which clinical efficacy has been demonstrated, is within the cost range acceptable by the NHS for routine medical interventions.

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PUBLICATION

Cutaneous malignant melanoma: Guidelines and practice

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Background: The Dutch Melanoma Working Party published guidelines for the management of malignant melanoma of the skin (last revision 1997 since 1984). According to these guidelines a diagnostic excisional biopsy must be followed by a therapeutic excision. In the histopathological report invasiveness of the tumour (thickness according to Breslow or depth of invasion according to Clark) and completeness of removal should be mentioned. We determined whether daily practice in 16 general hospitals served by 6 pathological laboratories was in line with these recommendations.

Methods: The Comprehensive Cancer Centre South ($\pm 1,000,000$ inhabitants) selected 578 patients (37% men and 63% women; mean age 51 years) who were reported to have a malignant melanoma of the skin by the six pathology-laboratories of the region in the years 1988, 1993 and 1997.

Results: In 85% of all patients diagnostic tissue was obtained by excisional biopsy. Completeness of removal was determined in 88%. Therapeutic excision was performed in 65% of patients. In 20% of these excisions a residue of the melanoma was found. Both diagnostic excisional biopsies as well as therapeutic excisions were performed in 53% of cases. In only 50% of all patients the complete procedure was according to the guidelines.

Conclusion: In daily practice guidelines for cutaneous melanoma were followed in about 50% of the patients in this registry. The precise background of the discrepancies is still under study.

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PUBLICATION

Simultaneous analysis of tyrosinase mRNA, L/DOPA and L/Tyrosine in the blood of patients with metastatic malignant melanoma

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The prognosis of malignant melanoma (MM) is based on the histological features of the tumor and clinical presentation. At the present time, there is no laboratory test to provide additional information on prognosis and metastatic spread of melanoma cells. Several MM tumor markers in peripheral blood have been proposed including S100 protein, neuron-specific enolase, lipid-associated sialic acid, melanoma-inhibiting activity protein (MIA) and tyrosinase, an enzyme specific to melanocytes and Schwann cells and also an excellent molecular marker of melanoma cells because of its primarily expression limited to melanocytes.

Determination of blood tyrosinase mRNA by RT-PCR and markers of tyrosinase activity (L-DOPA/L-Tyrosine ratio) by HPLC have been proposed as biological tools for the detection of metastases in melanoma patients. We prospectively evaluated their significance and clinical value in a group of 29 stage III (n = 6) and IV (n = 19) melanoma patients and one with melanosis of Dubreuilh. L-DOPA/L-Tyrosine ratio was elevated in 30% of stage III, 41% of stage IV patients (range: 7.5 to 261.10⁵) and in melanosis of Dubreuilh (184.8) (reference values: 6-16.10⁵). Four patients (stage IV, evolutive disease) were positive for tyrosinase mRNA. Tyrosinase mRNA positivity, but not L-DOPA/L-Tyrosine ratio, was associated with disease progression (p < 0.009). The presence of tyrosinase mRNA in blood is more related to clinical status and poor prognosis than levels of melanin precursors, which reflect tumor burden.

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PUBLICATION

Primary vulvar melanoma: A clinicopathological study of 27 cases

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Purpose: A retrospective analysis of a series of all patients with Primary Vulvar Melanoma (PVM) was conducted to evaluate effects of initial therapeutic procedures on disease-free-survival and overall-survival.