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Docetaxel in combination with dacarbazine (DTIC) in patients with advanced melanoma: a phase II study of the Hellenic cooperative oncology group

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Background: Chemotherapy for advanced melanoma remains disappointing. The number of agents that are active in patients with metastatic melanoma is limited. The aim of the study was to evaluate the efficacy and safety of a new combination regimen consisted of docetaxel and DTIC, as first line chemotherapy, in advanced melanoma.

Patients and methods: Patients with advanced melanoma, including cerebral metastases, were eligible. Docetaxel 80mg/m², IV over 1h infusion, D1 and DTIC 400mg/m², IV over 45', D1+2, were given every 21 days for 6 cycles.

Results: 41 pts entered the study; 39 were assessable for response. Objective responses were seen in 10 pts (24%). Three of them achieved a CR and 7 a PR, while 8 pts demonstrated stabilization of their disease. After a median follow-up of 20 months, the median TTP was 7 months (0.5-22) and the median survival 10 months (1-28). The main toxicity (G3-4) was neutropenia, which occurred in 8 pts. Additional patients had reversible G3-4 toxicities including alopecia, nausea/vomiting and fatigue; 3 presented mild hypersensitivity reactions to docetaxel. No toxic death was noted.

Conclusion: The above combination is well tolerated and has definite activity in pts with advanced melanoma.

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US scan and sentinel node biopsy (SNB) in the diagnosis of nodal metastases in patients with melanoma

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Introduction: In our experience US of nodal basins proved to be very accurate in detection of node metastases >2 mm. This technique, in theory, could avoid a subgroup of clinical stage I melanoma patients unnecessary SNB. This study is aimed to challenge this hypothesis.

Patients and Methods: Our series consisted of 130 consecutive clinical stage I cutaneous melanoma patients (62 M, 68 F; mean age 50.5 ys). The tumor was sited in limb in 81 patients, trunk in 42 and head-neck region in 7. Patients underwent preoperative US and FNAC (if nodal mets were suspected) and preoperative Tc99m-nanocolloid lymphoscintigraphy the day before surgery. Patent blue dye was intradermally injected at the tumor site 20 minutes before skin incision. Any SN(s), identified as blue stained and/or hot spot (hand-held gamma probe), were sent to the pathologist for E-E and immunohistochemistry (s-100 and HMB-45) sectioning. All the patients with positive findings at US and/or SNB underwent radical node dissection.

Results: SNB was performed in 143 basins, as 13 patients had dual-drainage at lymphoscintigraphy: 41.6% were in the axilla, 52.8% in the groin and 5.6% in the head-neck region. Patent blue dye with intraoperative lymphoscintigraphy allowed the identification of SN(s) in 98.6% of cases. Twenty-nine patients (22.3%) had lymph node metastases (31 basins). US findings were positive for 11 of the 31 metastatic basins (35.5%). Among the patients with positive US, nodal involvement was found partial in 8, massive in 2 and extranodal in 1, whereas, among the US negative cases, 11 had micrometastases, 8 partial and 1 extranodal metastases.

Conclusions: US +/- FNAC has an important impact on melanoma patient selection, allowing the identification of more than one-third basins with metastatic deposits (its main drawback being the resolution power of the probe), in which SNB is unnecessary.

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Detection of nodular and superficial spreading melanoma ≤ 2 mm – An interview study

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Purpose: To investigate differences in signs and symptoms between nodu-

lar melanoma (NM) and superficial spreading melanoma (SSM) with a tumour thickness ≤ 2.00 mm and factors for seeking medical attention.

Material and Methods: Semi-structured interviews with 22/25 patients with NM (all patients in the Stockholm-Gotland Regional Cancer Registry with NM ≤ 2.00 mm, diagnosed between 1994–1999 and still alive). A comparison group of 32/35 patients with SSM diagnosed during the same period, matched to the NM on age at diagnosis, gender and tumour thickness.

Results: NM were smaller in diameter than SSM according to patients' reports. NM were more often described as a new lesion than SSM. No other statistically significant differences between NM and SSM were found. The median time from detection to diagnosis was 4 months (range 1 day to 18 months) for NM and 6 months (1 week to 3 years) for SSM. In 61% the melanoma was detected by the patient herself/himself, but in 17% of the cases a family member or a friend was involved in the detection. The most important reason to seek medical attention (65%) was a change in the lesion or a symptom. 35% took the opportunity to show or ask about the lesion while at a doctors office for other reasons. 52% were encouraged by others to seek medical attention. In four cases, a physician detected the melanoma.

Conclusion: The results have implications for prevention of melanoma. Early detection of NM appears possible, provided that it is emphasised in public education that melanoma may have a diameter < 6 mm. Strategies for involving family members should be elaborated, since they play an important role in detection of melanoma and in motivating medical advice.

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Locally advanced uveal melanoma: primary and postoperative external radiotherapy

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Purpose: The effect of external radiotherapy on local control and survival in patients with locally advanced uveal melanoma was analysed retrospectively.

Material and Methods: Eleven patients (4 men, 7 women) with an median age of 69.8 years (range, 48.6–82.2) were treated at the Div. of Radiotherapy between 1987 and 1998. External radiotherapy either was given postoperatively (n=7) in advanced tumours with infiltration in adjacent structures or primarily in medical inoperable patients (n=2) and in patients with local recurrence following enucleation (n=2). A total dose of 40–56 Gy was used with single doses of 3–4 Gy.

Results: Mean follow-up was 38.2 months, (mean, 20.1; range, 5.4 to 94.7 months). The 5-year-disease-free, disease-specific and overall survival according to Kaplan-Meier were 33.7% (95% Confidence Interval, CI, 5–67), 43.8% (95% CI, 12–73) and 27.2% (95% CI, 5–54), respectively. Local control was achieved in all seven postoperatively irradiated patients. In three out of four primary irradiated cases, tumour regression could be obtained with complete remission in one of them. No severe radiation late effects were obtained.

Conclusion: Postoperative external radiotherapy is effective to achieve local tumour control also in patients with advanced local disease, however metastasis rate remains high. Radiation also has a potential as a primary treatment in selected inoperable patients or recurrent tumours by improving quality of life in those very cases.

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The role of serum S-100 protein and tyrosinase RT-PCR in staging patients with malignant melanoma

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Background: Staging of patients with malignant melanoma (MM) is crucial to determine prognosis and for planning adjuvant treatment. Unfortunately, there is no good clinical method to detect systemic micrometastases in patients with stage III disease.

The aim of this study was to evaluate the usefulness of serum S-100 protein and tyrosinase RT-PCR in detecting systemic micrometastases in patients with MM.

Patients and methods: From June 2000 to March 2001 measurement of S-100 protein and tyrosinase RT-PCR from peripheral venous blood was