Results: The median tyrosine hydroxylase mRNA in 12 of 12 melanoma cell lines was 0.000383 transcripts/cell (range 0.000012-0.005340 transcripts/cell). In neuroblastoma cells the median tyrosine hydroxylase mRNA number was 0.4 transcripts/cell (range 0.02-25 transcripts/cell). The results should also be compared with earlier found median transcript concentrations of four melanocyte-specific proteins, which varied between 116 and 435 transcripts/cell in the pigmented melanoma cell lines, and between 0.7 and 11 transcript/cell non-pigmented melanoma cell lines.

Conclusions: Less than 1 of 1000 melanoma cells contains any tyrosine hydroxylase mRNA. This is so low a number that the enzyme can not be produced effectively. Thus, pterin-dependent tyrosine hydroxylase can not be present in melanoma cells and does not contribute to pigment formation by producing any priming amounts of L-dopa for proper function of tyrosinase in human melanoma cells.

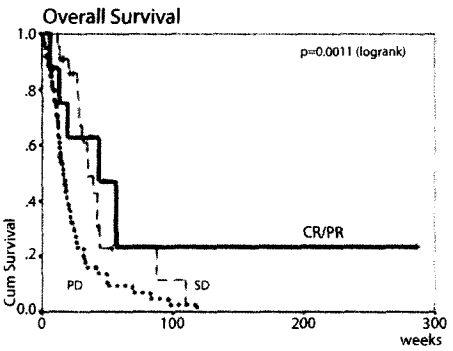
834 POSTER

Second-line treatment of disseminated malignant melanoma with Fotemustine

M. Weichenthal[1], M. Weichenthal[8], K. Neuber[2], P. Mohr[9], U. Trefzer[3], M. Fluck[10], J. Ulrich[4], J.C. Becker[5], U. Reinhold[6], M. Volkenandt[7].
[1] University of Kiel, Dept. of Dermatology, Kiel; [2] University of Hamburg, Hamburg; [3] University of Berlin, Berlin; [4] University of Magdeburg, Magdeburg; [5] University of Würzburg, Würzburg; [6] University of Homburg, Homburg; [7] University of Munich, Munich; [8] St.Georg Hospital, Hamburg, Germany; [9] Buxtehude Hospital, Germany

In a retrospective analysis, the role of the nitrosourea Fotemustine in the second-line treatment of disseminated malignant melanoma was evaluated. The multicentric study included a thorough review of patient's charts treated with Fotemustine during the period 1992-2002 in 11 melanoma centers in Germany.

A total of 91 patients (43m, 48f) aged 29-87 years (median 65y) could be identified who were treated for melanoma metastasis with intraveneous Fotemustine after relapse in first-line therapy. First line therapy often consisted of single agent DTIC (37%), temozolomide (13%), or combined DTIC/immunotherapy (18%). Eight patients had received polychemotherapy containing nitrosoureas. 38 patients (42%) had progressed with brain metastasis. Fotemustine was applied 100mg/sqm i.v. weekly for 3 weeks, and evaluation usually took place at day 50. In stable or responding patients a maintenance treatment was initiated. Seven of the patients with brain metastasis received a simultaneous total brain irradiation



In 8.8% of the patients an objective response could be achieved. Responses lasted from 4 to 285 weeks (median 23.5 weeks) and responding patients showed prolonged overall survival (Fig.1). The extent of metastatic disease appeared as a major prognostic factor, specifically when only 1 or 2 organs were affected. The presence of brain metatastasis had limited prognostic impact in this group of patients (Table 1).

Side effects were moderate and mainly affected the haematologic system with grade III/IV thrombopenia in 28 (30.8%), neutropenia in 19 (20.9%), and anemia in 11 (12.1%) of the patients. Further side effects included mild to moderate liver toxicity, and in some cases nausea.

In conclusion, Fotemustine can safely be administered as second-line therapy with some degree of antitumour activity in patients with metastatic malignant melanoma.

Abstract 834: Table 1: 2nd-line Fotemustine - single agent - iv

	n	OS (95% CI) [weeks]	CR (%)	PR (%)	OR (%)
Total	91	21.7 (14.9; 28.6)	2 (2.2%)	6 (6.6%)	8 (8.8%)
Tumor load					
Limited disease	19	31.9 (19.1; 44.7)	1 (5.3%)	2 (10.5%)	3 (16.8%)
Extensive disease	72	20.1 (16.0; 24.3)	1 (1.4%)	4 (5.6%)	8 (7.0%)
Metastaic sites					
1	21	31.9 (6.88; 56.8)	2 (9.5%)	4 (19%)	6 (28.5%)
2	27	35.4 (8.76; 62.1)	-	2 (7.4%)	2 (7.4%)
3	20	18.4 (8.19; 28.7)	-	-	-
4+	23	18.0 (9.93; 26.1)	-	-	-
Brain mets w/wo TBI	38	22.0 (13.1; 30.9)	1 (2.6%)	1 (2.6%)	2 (5.2%)
With radiation	7	34.4 (0; 71.8)	-	1 (14.3%)	1 (14.3%)
without radiation	31	22.0 (1; 26.4)	1 (3.2%)	-	1 (3.2%)

OS: overall survival; CI: confidence interval; CR: complete remission; PR: partial remission; OR: objective response; TBI: total brain irradiation

835 POSTER

Primary mucosal malignant melanoma - a retrospective single centre study

N. Costa, V. Angélico, M. Soares, I. Azevedo, J. Dinis, M. Lopes, C. Azevedo. *Portuguese Institute of Oncology, Medical Oncology, Porto, Portugal*

Background: Primary mucosal melanomas (MM) are rare, far fewer in number than melanomas of the skin. They manifest a more aggressive biologic course and such behaviour attends melanomas at any mucosal site. The authors study population characteristics, prognostic factors, and survival.

Material and methods: This study was performed retrospectively to include all cases of MM seen at the Portuguese Institute of Oncology, Oporto, Portugal, between 1984 and 2002. A total of 52 patients were reviewed. Clinical data was extracted from each patient's records. After excluding patients on who m most clinical information was unavailable (n=5), 47 patients remained for analysis. Primary anatomic site of MM, the symptoms and signs that brought him/her to the doctor, the clinical stage at presentation, the treatment modality and the outcome, were analyzed. The data related to the macroscopic and microscopic characteristics of the lesion were obtained from the pathologist original report. Overall and disease-specific survival, were calculated using the Kaplan-Meyer method, and univariate survival analysis was performed using the log-rank test.

Results: Forty -seven cases of Caucasian MM form the basis of this study. There were 13 men (27,7%) and 34 women (72,3%), with a median age of 66 years (33-86). Seventeen patients (36,1%) had MM of the head and neck (MMHN), 20 patients had MM of the genitalia (42,6%) and 10 patients had primary anorectal melanoma (21,3%). Regarding the patients with MMHN, the primary tumour arose in the oral cavity in 9 (53%) and the nasal cavity in 8 (47%). Within the oral cavity, 43% lesions involved the palate. The origin of the MM of the genital tract was: vulva, 13 patients (65%) vagina, 7 (35%). The anorectal melanoma patients were distributed by anal, 7 patients (70%) and rectum, 3 patients (30%). Among the 17 patients with MMHN, 13 patients (76,4%) had Stage I or localized disease, 4 (23,5%) had Stage II or locoregional disease and none had Stage III or distant disease at presentation. Clinical stages at presentation for genital tract melanoma were assigned as follows: Stage I, local disease only, 13 patients (65%); and Stage II, regional disease, 7 patients (35%). The 10 patients with anorectal melanoma comprehended 3 patients (30%) with localized disease, 4 (40%) with regional lymph node metastases and 3 (30%) with distant metastases at presentation.After developing symptoms, the median time to diagnosis was 11 months (1-84). The median follow-up time was 24 months (0,3-125), with an overall survival (OS) of 27 months (12-42). Attending the mucosal site OS analysis revealed59 months (±15) for MMHN, 56 months (±13) for MM of the genitalia, and 10 months (±5) for anorectal MM. Univariate survival analysis were performed within each of the former groups, and for none of the tested risk factors we achieved a significant value.

Conclusions: The outcome is poor, with 5-year OS well below 50% (35% in our study). Among prognostic factors, only the anatomic site of origin showed significant influence in survival (p=0,02).