and NRAS mutated metastatic melanoma. Two Cdk inhibitors, which target Cdk2/Cdk4 and Cdk4/Cdk6, have been selected for further analysis to evaluate these cyclin dependent kinases as novel therapeutic targets for the treatment of metastatic melanoma.

Table1: Effective Cdk inhibitors in two melanoma cell lines

Inhibitor	Sk-Mel-28% Inhibition (± std dev)	Sk-Mel-2% Inhibition (± std dev)
Alsterpaullone, 2-Cyanoethyl (Cdk1/5; GSK-3b)	65.6± 13.0	64.5± 4.1
Cdk1/2 Inhibitor III	99.9± 0.0	98.0± 1.0
Cdk4 Inhibitor III (Cdk2/4)	72.6± 22.8	53.9± 8.5
Cdk/Crk Inhibitor	99.8± 0.0	99.6± 0.2
Fascaplysin (Cdk4/6)	99.2± 0.6	98.0± 1.0

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Expression of cancer-testis antigens is a poor prognostic factor in primary but not metastatic melanoma

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Background: Cancer-Testis Antigens (CTAg) are commonly expressed in melanoma. Their immunogenicity and limited normal tissue expression make them attractive targets for anti-cancer immunity. Using three CTAg against which vaccines have been developed, we evaluated whether CTAg expression is a prognostic factor in cutaneous primary and metastatic melanoma.
Methods: Expression of MAGE-A1, MAGE-A4 and NY-ESO-1 by immunohistochemistry was evaluated in 233 stage II (primary) and 261 stage III/IV (metastatic) melanoma samples. Univariate analysis (UVA) was performed by the Kaplan-Meier method using the log-rank test. Multivariate analysis (MVA) using CTAg expression and known prognostic factors was performed by the Cox proportional-hazards regression model.
Results: Expression of at least 1 CTAg (CTAg+ve) was a poor prognostic factor in stage II melanoma, with median relapse-free survival (RFS) of 72 months for CTAg-ve tumours *vs.* 45 months for CTAg+ve tumours ($p = 0.008$). On UVA, CTAg expression, ulceration, Breslow thickness and mitotic rate were identified as prognostic factors. MVA demonstrated that the prognostic impact of CTAg expression in primary melanoma was comparable to ulceration and Breslow thickness, both currently accepted prognostic factors (Table). CTAg expression was not a prognostic factor in stage III/IV melanoma with median overall survival of 23 months each for CTAg+ve and CTAg-ve tumours ($p = 0.72$). The prognostic significance of tumour stage, performance status (PS) and LDH, all of which are known prognostic factors in metastatic melanoma, was confirmed on UVA and MVA (Table).

Cox proportional-hazards regression analysis

Parameter	Subgroup	p-value	Hazard ratio (95% confidence interval)
Stage II (primary) melanoma			
Any CTAg	positive or negative	0.010	1.72 (1.14−2.58)
Ulceration	Present or absent	0.008	1.80 (1.17−2.77)
Breslow thickness	>4.0 mm or <4.01 mm	0.003	1.87 (1.24−2.81)
Mitotic rate	$\geqslant 4\,mm^2$ or $0\,mm^2$	0.14	1.91 (0.82−4.44)
Stage III/IV (metastatic) melanoma			
Any CTAg	positive or negative	0.71	0.93 (0.64−1.36)
Stage	IV or III	0.02	1.60 (1.08−2.38)
PS	ECOG 2+ or 0−1	<0.001	3.27 (1.80−5.94)
Serum LDH	High or normal	<0.001	2.64 (1.72−4.04)

Conclusion: CTAg expression was a significant prognostic factor in primary but not metastatic melanoma. The prognostic impact of CTAg expression in cutaneous primary melanoma was comparable to Breslow thickness and ulceration. Further study into CTAg function and the impact of clinical targeting is warranted.

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Radical radiotherapy for clinically localized sebaceous carcinoma of the eyelid: a retrospective analysis of 78 patients

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Background: To analyze retrospectively the results of radiotherapy for clinically localized sebaceous carcinoma of the eyelid.
Materials and Methods: The records of 78 patients with histologically confirmed sebaceous carcinoma who were treated between 1983 and 2007 were reviewed. Patients with distant metastasis and/or lymph node metastasis at initial diagnosis were excluded in this study. All 78 patients were treated with radical radiotherapy to the primary tumor (electron beams: 74 patients; X-ray: 4 patients) and the total radiation doses ranged from 30.0 to 70.4 Gy (median: 60.0 Gy). The median follow-up of all patients was 64.8 months (range, 2.8−270.3 months). Overall survival (OS), disease-free survival (DFS) and local control (LC) rates were calculated actuarially according to the Kaplan-Meier method, and differences between groups were estimated using the log-rank test. Multivariate analysis was performed using the Cox regression model.
Results: At the time of analysis, 10 patients (12.8%) died, and local recurrence was observed in 31 patients (39.7%). The 5-year actuarial OS, DFS and LC rates for all patients were 89.6%, 54.3% and 58.4%, respectively. Patients with T1−2 tumors had a significantly higher LC (5-year LC: 74.2%) than those with T3−4 tumors (5-year LC: 40.0%; $p = 0.014$). Multivariate analysis indicated that T stage alone was a significant prognostic factor for LC. Concerning DFS, patients with T1−2 tumors had a significantly higher DFS (5-year DFS: 71.5%) than those with T3−4 tumors (5-year DFS: 34.1%; $p = 0.0071$). Multivariate analysis indicated that T stage alone was a significant prognostic factor for DFS. Late morbidity of CTCAE Grade 3 was observed in only 1 patient (eyelid dysfunction).
Conclusions: These results indicate that radical radiotherapy is the treatment of choice for early-stage (T1−2) sebaceous carcinoma of the eyelid. On the other hand, multimodal treatment may be recommended for advanced (T3−4) disease.

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Efficacy of a hypofractionated schedule in electron beam radiotherapy for epithelial skin cancer: analysis of 434 cases

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Background: To evaluate the efficacy of radiation therapy for epithelial skin cancer and compare treatment outcomes of two electron beam fractionation schedules.
Material and Methods: Outcome data of 434 epithelial skin cancers in 333 patients, treated between 2001 and 2006 were analysed. 332 were basal cell carcinomas (BCC) and 102 squamous cell carcinomas (SCC). Patients were treated with electron beam irradiation for primary skin cancer ($n = 386$) or after previous resection ($n = 48$), and received either 54 Gy in 18 fractions ($n = 159$) or 44 Gy in 10 fractions ($n = 275$), 4 fractions per week. A pilot study was performed to evaluate cosmetic outcome in 14 patients. Local recurrence free rates (LRF) were analysed using the competing risk method. Secondary endpoints were metastases free rates, cancer specific survival (CSS) and cosmetic result.
Results: Median follow up was 42.8 months. Actuarial 3-year LRF rates were 97.5% and 96.1% for 54 Gy and 44 Gy, respectively. For BCC, 3-year LRF rates were 97.6% for tumours treated with 54 Gy and 96.9% for those treated with 44 Gy. In SCC 3- year LRF rates were 97.0% for 54 Gy and 93.6% for 44 Gy (n.s.). T stage was found to be a significant factor for recurrence ($p = 0.036$). No significant differences in LRF rates were found for fractionation schedule, age, histology, primary or postsurgical treatment, or tumour location. In 5 patients with SCC metastases were diagnosed. Three-year CSS was 98% for SCC and 100% for BCC. Cosmetic outcome was scored 'good' or 'fair' by 75% of patients and 87% of objective observers in the 54 Gy group and 100% and 83% in the 44 Gy group.
Conclusions: Electron beam irradiation is a safe and effective treatment modality for epithelial skin cancer, and can be recommended both for primary treatment in cosmetically sensitive areas, and after surgery in case of involved margins. Local control rates greater than 95% are found for T1 and T2 tumours. In view of the similar efficacy and patient convenience of the hypofractionated schedule, 44 Gy in 10 fractions can be regarded the radiation schedule of choice, especially in elderly patients.