**7005** ORAL

**Ipilimumab (MDX-010) in patients with stage III/IV melanoma: kinetics and duration of response**

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**Background:** The fully human monoclonal antibody ipilimumab (MDX-010) blocks cytotoxic T-lymphocyte antigen-4 (CTLA-4) and enhances immune responses to tumor-associated antigens resulting in durable objective responses (ORs). This abstract reviews data from 5 studies (2 complete and 3 ongoing) and describes the kinetics and duration of response after ipilimumab treatment.
**Materials and Methods:** A total of 269 treated patients with stage III/IV melanoma were reviewed and analyzed to determine the kinetics and duration of response after ipilimumab. Ipilimumab doses ranged from 0.3−10 mg/kg/dose (single or multiple). Patients received ipilimumab alone or with dacarbazine, IL-2 or gp100 peptide vaccine. Complete and partial response (CR, PR), stable and progressive disease (SD, PD) were evaluated.
**Results:** Overall, 15% of patients (N = 41) had a confirmed OR at analysis. Late onset responses occurred in some patients: CR from ~10–106 weeks and PR from ~5−62 weeks post-treatment initiation. In 28 patients, onset of CR or PR occurred after >~12 weeks of treatment. PD preceded OR (without additional therapy) in 4 patients. In 2 patients, PD measured at ~6 weeks post-treatment initiation was followed by a PR at ~12 weeks. In 1 of these patients the PR changed to a CR at ~24 weeks and lasted for ~188 weeks+; the other patient maintained a PR for ~17 weeks. In the other 2 patients, PD at ~12 weeks was followed by SD at ~17−20 weeks and a PR after ~30 and 62 weeks. PRs in both patients lasted for ~17 and 40 weeks+, respectively. Duration of OR ranged from ~6–187 weeks+; ORs are ongoing in 25 patients. Late onset occurred irrespective of dose, regimen and therapeutic partner.
**Conclusions:** These preliminary results suggest that ORs with ipilimumab may be later in onset and more durable than with traditional chemotherapy. They also may occur after disease progression. Late onset of effect likely reflects the immune-related mechanism of action of ipilimumab. This suggests that continued treatment or observation may be beneficial despite initial PD or SD.
**Acknowledgement:** Dr. S. Rosenberg

**7006** ORAL

**Prognosis depends on micro-anatomic patterns of melanoma micrometastases within the sentinel node (SN). A multicenter study in 388 SN positive patients**

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**Background:** The SN procedure has become the standard staging procedure for stage I/II melanoma patients (pts). The basis of the sensitivity of this procedure is the number and site of step sections in the pathology protocol used for the work-up of the SN [Cook et al., J Pathol 2003 Jul; 200(3): 314−9]. The more intensive the pathologic workup, the higher the SN positivity rate. This increase is also characterized with an increased detection of cases with only minimal tumor burden, which represents different biology.
**Methods:** In the framework of the EORTC Melanoma Group the slides of positive SN of 388 patients from three cooperating centers have been reviewed and analyzed. Slides were reviewed for the location of the metastasis within the SN (Dewar et al., J Clin Oncol 2004; 22: 3345−9) and classified according to the Rotterdam Classification of Tumor Burden (<0.1 mm; 0.1−1 mm; >1 mm) maximum diameter of the largest metastasis (van Akkooi et al., Ann Oncol 2006; 17: 1578−85). The predictive value for additional nodal metastases in the completion lymph node dissection (CLND) and disease outcome as disease free (DFS) and overall survival (OS) were calculated.
**Results:** The study included 388 pts, 95 (25%) from Rotterdam, 86 (22%) from Berlin and 207 (53%) from Warsaw. Median age was 51 years and 53% was female. 49% of primary tumors were located on an extremity, 48% on the trunk and 3% were head & neck tumors. Mean and median Breslow thickness was 5.25 and 4.00 mm. Ulceration was present in 56% of primary tumors. 40 pts (10%) had metastases <0.1 mm., 69 pts (18%) had metastases confined to the subcapsular space. Additional nodal positivity was seen in only one of the 40 pts with metastases <0.1 mm. Mean and median follow-up was 34 and 28 months. 5-year estimated OS for metastases <0.1 mm was 91%, 0.1−1.0 mm was 62% and >1.0 mm was 48%.
**Conclusion:** Different pathology protocols yield different rates of minimal SN tumor burden. In the two centers with very similar protocols there was a virtually identical rate of 20% of SUB-micrometastases (<0.1 mm). This study validates in a large multicenter patient group (almost 2 times more node positive pts than in the MSLT-1 trial) that the observation that patients with SUB-micrometastases have excellent prognosis that does not seem to differ from SN-negative pts.

## *Poster presentations* (Tue, 25 Sep, 14:00−17:00)
## Melanoma and skin cancer

**7007** POSTER

**Development of antigen microarray for systematic analyses of humoral responses in melanoma patients**

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**Background:** There is no doubt that autoantibodies against tumor-derived proteins may reveal novel targets for immunotherapy and genes relevant for tumor etiology. Growing body of evidence suggests them also as valuable tool for early detection of cancer and prediction of disease and immunotherapy outcomes. Great diversity in antigen repertoires and frequencies among individual patients and tumors raises the need to identify high numbers of antigens to ensure selection of most relevant biomarker candidates. The aim of the study was to identify majority of serum-reactive proteins in melanoma and to develop antigen microarray applicable for systematic analyses of autoantibody signatures in melanoma patients.
**Material and Methods:** Antigen identification comprised construction of cDNA expression libraries using T7Select® phage surface cloning system, enrichment of the libraries for serum-reactive clones via biopanning with melanoma patients' sera and immunoscreening of the libraries. All serum-reactive phage clones were isolated and encoded antigens identified by sequencing. Antigen microarray was generated by printing antigen-encoding phages onto nitrocellulose-coated glass slides by Genetix QArraymini printer.
**Results:** One testis and five melanoma cDNA expression libraries were constructed and immunoscreened with 25 melanoma patients' sera resulting in the identification of ~900 serum-reactive clones representing 518 different antigens. Among them there are known CT antigens, such as NY-ESO-1, SSX2, GAGE and MAGEA family members, known tumor antigens previously identified with serological expression cloning and several gene products previously unknown as antigens. Nevertheless, in more than 85% cases antigens are translated in other reading frames or represent mtDNA, untranslated or intergenic regions and likely mimic epitopes of other, yet unknown antigens. A set of 518 antigens were printed on glass slides and the antigen microarray was tested with 20 healthy donor and melanoma patients' sera. These experiments revealed that phage clones retain their reactivity with serum antibodies after immobilisation on glass slides; moreover, a subset of candidate autoantibodies capable to discriminate cancerous from non-cancerous was defined.
**Conclusions:** A melanoma antigen microarray was developed suitable for high throughput survey of autoantibody profiles in cancer patients. Further experiments will be performed to assess sensitivity and specificity of the assay.