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Antibodies as biomarker candidates for response and survival to checkpoint inhibitors in melanoma patients

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BACKGROUND
Long-term survival of stage IV melanoma patients has improved significantly with the development of immune checkpoint inhibitors (CIs). Reliable biomarkers to predict response and clinical outcome are needed.

METHODS
We investigated the role of melanoma-associated antibodies as predictive markers for CI therapy in two independent cohorts. In cohort 1, a prospective study, we measured specific antibodies before treatment, after one week and after six to nine weeks of treatment. Cohort 2 consisted of serum samples prior to CI therapy initiation. ELISA assays were performed to quantify specific IgG directed against melanocyte differentiation antigens tyrosinase-related proteins 1 and 2 (TRP1/TYRP1 and TRP2/TYRP2), glycoprotein 100 (gp100), MelanA/MART1, and the cancer-testis antigen NY-ESO-1. Response was defined as either complete or partial remission on CT scan according to RECIST 1.1.

RESULTS
In cohort 1, baseline levels of these antibodies were higher in the responder group, although statistical significance was only reached for NY-ESO-1 (p = 0.007). In cohort 2, significantly higher antibody baseline levels for MelanA/MART1 (p = 0.003) and gp100 (p = 0.029) were found. After pooling the results from both cohorts, higher levels of MelanA/MART1 (p = 0.013), TRP1/TYRP1 (p = 0.048), TRP2/TYRP2 (p = 0.047) and NY-ESO-1 (p = 0.005) specific antibodies at baseline were independently associated with response.

CONCLUSIONS
Melanoma-associated antibodies may be candidate biomarkers for response and survival in metastatic melanoma patients being treated with CIs. These markers may be used to complement patient assessment, in combination with PD-L1 status, tumor-infiltrating lymphocytes and tumor mutational burden,

with the aim to predict outcome of CI treatment in patients with metastatic melanoma.

TRIAL REGISTRATION
Ethikkommission Ostschweiz, EKOS 16/079 https://ongoingprojects. swissethics.ch/runningProjects_list.php?q=%28BASECID~ contains~2016-00998%29&orderby=dBASECID .