Biomarker analysis from the OpACIN trial (Neo-/adjuvant ipilimumab + nivolumab (IPI+NIVO) in palpable stage 3 melanoma)

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**Background**
- The outcome of high risk stage 3 melanoma patients is poor (20-59% 5-year survival).1,3
- Adjuvant ipilimumab (IPI, anti-CTLA-4) improved 5 year recurrence-free survival (RFS) and overall survival (OS).4
- Adjuvant nivolumab (NIVO, anti-PD-1) improved RFS compared to IPI.5
- The combination of ipilimumab plus nivolumab (IPI+NIVO) improved objective response rates (ORR), progression free survival (PFS), and OS significantly compared to IPI and numerically compared to NIVO.6
- Neo-adjuvant treatment (before surgery) might be more favorable, as immune checkpoint inhibition (ICI) is of greatest value at the moment of T-cell receptor (TCR) triggering and thus dependent on the amount of antigen present.
- Thus, we postulated that adjuvant immunotherapy will work most efficiently, when immunotherapy is initiated prior to surgery.

**Methods**
- The OpACIN trial is a two-arm randomized phase 1b feasibility trial in 20 high risk AJCC stage 3 B/C melanoma patients with palpable nodal disease.
- Patients received the combination of IPI 3mg/kg plus NIVO 1mg/kg, either adjuvant 4 courses after surgery, or 2 courses neo-adjuvant and 2 courses adjuvant.
- Co-primary objectives were safety, feasibility, and the comparison of the immune-activating capacity of neo-adjuvant versus adjuvant IPI+NIVO.
- Median follow-up post-surgery is 17 months (date last October 2017)

**Clinical Results**

**Safety and Feasibility**
- All patients in the neo-adjuvant arm underwent lymph-node dissection on the pre-planned time-point.
- The grade 3/4 adverse event rate was 90% and did not differ between both arms.
- Only 2/20 patients received all four courses (17 patients stopped due to toxicity and 1 due to PD after two courses adjuvant).

**Efficacy**
- Pathological response rate was 80% in the neo-adjuvant arm.
- At a median follow-up of 18.6 months, 6 patients relapsed.
- 2/20 (10%) patients in the neo-adjuvant arm relapsed.
- 4/10 (40%) patients relapsed in the adjuvant arm.

**References**
- Eggertsen et al., NEJM 2016.
- Lamkin et al., NEJM, 2015.