still treated according to a "one size fits all" approach. While tumor staging offers some stratification, the development of personalized treatment concepts remain elusive. Our group has recently validated the Proactive Molecular Risk Classifier for Endometrial Cancer (ProMisE), to distinguish clinically relevant prognostic groups. ENOC shares risk factors, genomics, and histology with it's endometrial counterpart. The aim of our study was to apply and investigate ProMisE in ovarian endometrioid carcinoma.

Methods ProMisE was applied to n=509 ENOC after biomarker-assisted review of endometrioid histotype. Cases were aligned into four groups: low risk POLE mutant (POLE); moderate risk mismatch repair deficient (MMRd); high-risk p53 abnormal (p53abn); and a final moderate risk category lacking these biomarkers (p53wt). Kaplan-Meier and multivariable survival analyses were performed.

Results 4% of cases were POLE, 16% MMRd, 10% p53abn and 71% p53wt. Groups showed distinct progression-free and overall survival (p<0.001), near-identical to profiles of endometrial carcinoma. 5-year PFS was 54% in p53abn, 81% in MMRd, 84% in p53wt, and 100% in POLE cases. ProMisE classes of ENOC were independent of stage and residual disease in multivariable analysis.

Conclusions ProMisE risk classification provides additional prognostic information in a large cohort of ENOC. Our findings support the introduction of ProMisE-stratified treatment algorithms to ultimately improve endometrioid ovarian carcinoma patient care. Further, ENOC may benefit from parallel efforts under investigation in endometrial carcinoma.

IGCS19-0177

4 PROGNOSTIC IMPACT OF TUMOR INFILTRATING NATURAL KILLER CELLS IN OVARIAN CARCINOMA

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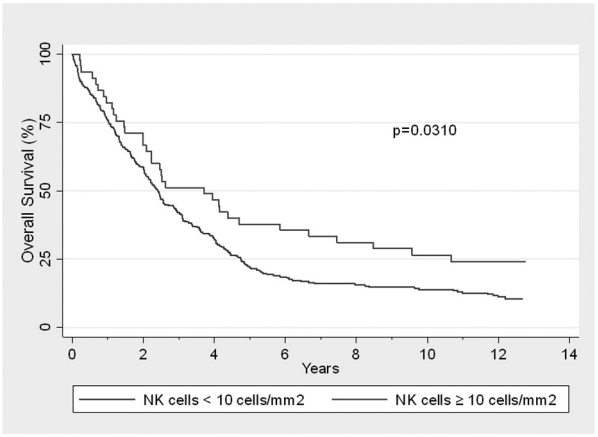
Objectives Whereas the prognostic impact of infiltrating T cells in ovarian cancer is established, the impact of other immune cells is largely unknown. The aim of the present study was to investigate the prognostic impact of intratumoral T cells, Natural Killer (NK) cells, neutrophils and PD-L1 expression.

Methods All patients diagnosed with high-grade serous carcinoma (HGSC) in Denmark in 2005 were included in the study (N=283). Immunohistochemical staining with antibodies for PD-L1, T cells (CD8), neutrophils (CD66b), and NK cells (CD57) were performed. Cell densities were analyzed using a digital image analysis method. The primary endpoint was overall survival (OS).

Results In patients with high levels of tumor infiltrating NK-cells the median OS was 45 vs 29 months (figure 1).



Abstract 4 Figure 1 NK cells high-grade serous carcinoma

The median OS was 37 vs 25 months (p=0.0008) for high vs low level of tumor infiltrating T cells, respectively. In multivariate analysis high numbers of NK-cells and T-cells remained independent markers of favorable OS with hazard ratios of 0.72 (p= 0.020) and 0.67 (p=0.041) in favor of high T cell and high NK cell density respectively. A high level of PD-L1 expression was associated with improved OS (37 months vs 22 months, p=0.0006). PD-L1 was only borderline significant in the multivariate analysis (HR 0.77, p=0.061). Neutrophils had no significant association with OS.

Conclusions This population based cohort study demonstrated a favorable prognostic impact of high levels of tumor infiltrating NK-cells in patients with HGSC, and confirmed the importance of tumor infiltrating T cells. This may influence the future development of immunotherapy in ovarian carcinoma.

IGCS19-0726

5 THE GOOD PROGNOSIS OF IMMUNOREACTIVE SUBTYPE OF HIGH-GRADE SEROUS OVARIAN CANCER (HGSOC) IS NEGATIVELY IMPACTED WHEN OBESITY AND LIPID METABOLISM-RELATED GENES ARE HIGHLY EXPRESSED

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Objectives HGSOC is the deadliest gynecologic cancer. Molecular analysis to samples available at The Cancer Genome Atlas (TCGA) allowed the identification of 4 molecular subtypes with different biology/prognosis. Recently, our group demonstrated by bioinformatic analysis that patients expressing high levels of genes related to obesity and lipid metabolism (e.g. CD36/TGFß) experienced poorer outcomes in two international cohorts (TCGA and AOCS). Here, our goal was to establish if there was correlation between such patterns and

the prevalence and prognosis of different molecular subtypes of HGSOC.

Methods We retrieved matching data of 455 cases of stage II-IV HGSOC from TCGA and categorized into 4 clusters based first on molecular subtypes (differentiated, immunoreactive, mesenchymal and proliferative) and then subdivided based on obesity and lipid metabolism gene pattern expression (CD36/TGFß high vs low). Proportion and survival analyses were carried out. Chi square, Kaplan Meier were used to assess statistical significance.

Results Mesenchymal subtype was significantly more prevalent among women expressing CD36/TGFß high (51,2% vs 6,9%, p<0.0001). Proliferative and differentiated were more prevalent in women expressing CD36/TGFß low (71,3% vs 27,7%, p<0.0001). The 5-year overall survival was significantly different between subgroups with the immunoreactive subtype expressing CD36/TFGß low experiencing the best outcome compared to the rest (median 67,7 vs 44,1 months, log-rank p<0.01). Cox analysis (including clustering, age, cytoreduction and therapeutic response) confirmed the immunoreactive CD36/TGß/low as independent prognostic factor.

Conclusions Our results confirm the importance of immune response and the negative impact that obesity and lipid metabolism alterations have in defining prognosis in HGSOC (supported by Fondecyt 1160800).

Plenary 2

IGCS19-0362

6 INTERPRETING IMMUNE INFILTRATES AND HORMONE BIOMARKERS IN YOUNG WOMEN WITH ENDOMETRIAL CARCINOMA (EC) THROUGH A MODER LENS (POST-TCGA) OF MOLECULAR CLASSIFICATION

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Objectives Approximately 15% of ECs are diagnosed in women before the natural age of menopause. Fertility-sparing conservative management options are increasingly utilized, however biomarkers to inform prognosis or direct therapy are lacking. We sought to determine the value of additional immunohistochemical biomarkers in young women with EC in the context of modern TCGA-based molecular classification.

Methods Allred scores for estrogen/progesterone/androgen receptor and Ki67 in addition to immune characterization measuring stromal and epithelial expression of CD3/CD8/CD79a/CD138/PD1 and TIL^{high} vs. TIL^{low} clusters was performed in a cohort of previously characterized(n=257) young women (<50yo) with EC. Testing for association of biomarkers with clinicopathological parameters, ProMisE molecular subtype (mismatch repair deficient (MMRd), *POLE* mutated (POLE), p53wildtype (p53wt) and p53abnormal (p53abn)) and outcomes was performed.

Results Young women had a high proportion of immune-rich ECs: 80% TILhigh compared with 60% TILhigh in non-age stratified cohorts. Expression of all immune biomarkers was enriched within POLE and MMRd subtypes. Within MMRd and p53wt ECs TILhigh immune cluster was associated with improved overall-(OS)and disease-specific survival (DSS)(p<0.05 for all). High ER and PR expression was associated with low-grade ECs, and increased PD1 expression. A trend (LRT p-value 0.1) towards improved OS(HR 0.4) and DSS(HR 0.273) in high PR-expression ECs was observed. Inconsistencies in progesterone treatment (dose, duration) precluded our ability to make firm conclusions on PR thresholds and efficacy. In multivariable analysis only ProMisE subtype showed independent prognostic significance.

Conclusions Molecular classification with additional selective biomarker testing can provide additional prognostic information and may help stratify young women with ECs for targeted therapies.

IGCS19-0185

7 EFFECT OF MEGESTROL ACETATE PLUS METFORMIN AS FERTILITY-SPARING TREATMENT FOR PATIENTS WITH ATYPICAL ENDOMETRIAL HYPERPLASIA AND WELL-DIFFERENTIATED ENDOMETRIAL CANCER. A RANDOMIZED CONTROLLED TRIAL

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Objectives The clinical remission (CR) rate of Megestrol acetate (MA) as fertility-sparing treatment was still not optimal. This study was to access whether MA plus metformin could lead to better CR rate for patients with atypical endometrial hyperplasia (AEH) and well-differentiated endometrial cancer (EC).

Methods This was a randomized, single-center, open-label and controlled trial (July 2013-December 2017). Patients were randomized to receive MA (160mg, orally, daily) or MA (160mg, orally, daily) plus metformin (500mg, orally, three times a day), then underwent hysteroscopy every 3–4 months. The primary efficacy parameter was the CR rates at 16th and 30th weeks of treatment (16w-CR rate and 30w-CR rate); the secondary efficacy parameter was rates of recurrence, pregnancy and live-birth.

Results Totally 150 patients received MA (n=74, 62 AEH and 12 EC) or MA/metformin (n=76, 61 AEH and 15 EC). The 16w-CR rates were 34.3% (23/67) and 20.7% (12/58) in MA/metformin- and MA-treated women (p=0.091). However, among 102 AEH patients, MA/