Serous tubo-ovarian carcinoma: Prognostication and early detection

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Background

Epithelial ovarian cancer (EOC) is histologically heterogeneous. The most common and deadly subtype is high-grade serous ovarian carcinoma (HGSOC), accounting for 70% of all EOC. Unfortunately, no great improvements in outcome have been made over the past decades. HGSOC are characterized by genomic instability, mutations in the tumor suppressor gene Tumor protein 53 (TP53) early in the malignant evolution and are proposed to arise in the tubal epithelium.

Aims and Methods

This project can be divided into two parts.

1. Potential prognostic and predictive biomarkers:

In the first publication Claudin-4 immunohistochemistry (IHC) was performed in a tissue microarray (TMA) including 128 patients with EOC.

In the second manuscript the immune markers CD3, CD68, PD-1 and PD-L1 were studied by IHC in another TMA comprising 141 patients with HGSOC. Follow-up studies in this cohort will include markers of macrophage and lymphocyte specificity (CD163 and FOXP3, respectively) and other immune checkpoint inhibitors.

2. Early detection:

The MaNiLa-project aims to develop a DNA-based diagnostic test for early detection of HGSOC. One of the approaches in this project is to explore the possibility of detecting cancer-derived TP53 mutations with IBSAFE™ technology in liquid vaginal smears collected a few years before the women have been diagnosed with HGSOC (third manuscript).
Abstract

Half Time Review, Laura Martin de la Fuente, 18th May 2018
Division of Oncology and Pathology, Department of Clinical Sciences, Lund

Preliminary results

The findings in the published article suggested that high expression of claudin-4 may have a prognostic value in EOC.

We identified a group with co-expression of PD-L1 in tumour-associated macrophages and PD-L1 in tumour infiltrating lymphocytes with significantly better prognosis, even after adjusting for clinical factors known to influence ovarian cancer survival in the second study.

In the MaNiLa-project and as a first step, we have detected 12 patients with TP53 mutations (of 67 patients with HGSOC) in vaginal smears taken at the time of diagnosis using ddPCR.

Significance

In the first part, we aim to stratify patients diagnosed with EOC and HGSOC based on phenotype and identify new predictive tools that could enable more successful application of new targeted drugs (e.g. PD-1/PD-L1 blockade therapy).

The presence of cancer-derived TP53 mutations in vaginal smears at the time of diagnosis, have been shown in previous studies. However, the detection in the pre-symptomatic situation is, to our knowledge, novel and unique.

Published work


Manuscripts

PD-1/PD-L1 expression and tumor-infiltrating lymphocytes are prognostically favorable in high-grade serous tubo-ovarian carcinoma. Laura Martin de la Fuente, Sofia Westbom Fremer, Linda Hartman, Nicolai Skovbjerg Arildsen, Susanne Malander, Päivi Kannisto, Anna Måsbäck and Ingrid Hedenfalk.