

# ABSTRACT

## **First part of the thesis: Prognostic factors influencing the effect of chemotherapy in ovarian cancer**

*INTRODUCTION:* Membrane transporter proteins (for example ABC, SLC and ATPases) take part in oncogenesis and the formation of chemoresistance, however the interpretation of their importance in ovarian cancer prognosis is still limited.

*METHODS:* Gene expression profiling was performed on 39 ABC and 12 SLC transporters and 3 ATPases in epithelial ovarian cancer (EOC) tissues and the results were assessed with respect to prognosis and clinical presentation of EOC patients. In a cohort of tissues with primary EOC (n = 57) and control tissues (n = 14) we assessed relative expression of genes and compared it with the clinical and survival information. The data was verified on a separate cohort (n = 60).

*RESULTS:* 6 ABC genes and the SLC22A18 gene were considerably over-expressed in the cancer tissues in comparison with control tissues and the expression of 12 ABC genes, 5 SLC genes, ATP7A, ATP11B was reduced. The expression of ABCA12, ABCC3, ABCC6, ABCD3, ABCG1, SLC22A5 genes was greater in HGSC in comparison with other types. Expression of ABCA2 was considerably related to tumour grade in both cohorts. Particularly, the expression levels of ABCA9, ABCA10, ABCC9 and SLC16A14 were considerably related to PFS in both pilot and verification groups. ABCG2 level was related to PFS in the grouped patient cohort.

*CONCLUSION:* The genes ABCA2, ABCA9, ABCA10, ABCC9, ABCG2 and SLC16A14 represent new potential markers of epithelial ovarian cancer progression and collectively with the discovered association between the expression of ABCA12, ABCC3, ABCC6, ABCD3, ABCG1, SLC22A5 and HGSC they should be investigated more extensively in future studies.

## **Second part of the thesis: Cervical cancer in young women – reduction of radicality in early stages**

*INTRODUCTION:* The common procedure for cervical cancer is radical hysterectomy (RH) and pelvic lymphadenectomy (LAP). Due to the growing age of women at delivery, fertility is becoming a key concern. Patients fulfilling the predefined criteria (stage IA1, LVSI positive, stage IA2 and stage IB1 (< 2cm and infiltration <1/2 of the stroma) were offered two-step less radical fertility-sparing surgery.

*METHODS:* The preoperative workup consisted of histopathological diagnosis and MRI with US volumetry. Subsequently, laparoscopic sentinel node mapping with intraoperative freeze biopsy was performed, followed by pelvic lymphadenectomy and, in case of negative results, "selective parametrectomy". If confirmed by definitive histology, women underwent simplex trachelectomy (IB1) or conisation (IA1/IA2) one week following primary operation.

*RESULTS:* Between 1999 and 2018, 91 patients were included in the study (median age 29.1, range 21-40 years). 51 (56.0 %) of these women were nulliparas. The detection rate of SLN was 100% per patient and the specific side detection rate was 96.7%. Nine cases (9.8%) were diagnosed with positive LN and RH was performed. Fertility was preserved in 80 patients, but 4 patients had local recurrence (5.0%). Mortality was 0.0%, median follow-up 149 months.

*CONCLUSION:* Less radical fertility-sparing surgery with SLNM is safe for cervical cancers <2 cm in greatest diameter with infiltration <1/2 cervical stroma. The rate of recurrence is acceptable and there was no mortality observed. This procedure has a low morbidity. Patients after this treatment however require extensive and accurate follow-up, in which testing for oncogenic high-risk HPV viruses and the possibility of vaccination appear to be beneficial.