Conclusion Expression of TROP-2 in cervical cancer is associated with increased levels of intratumoral TILs, indicating the potential therapeutic target for TROP-2 targeted antibody-drug conjugate alone or in combination with immune checkpoint inhibitors.

2022-RA-803-ESGO FUNCTIONAL CHARACTERIZATION OF NRIP1 IN ENDOMETRIAL CANCER; MUTATIONS ASSOCIATES WITH AGGRESSIVE FEATURES WHILE LOW EXPRESSION LEVELS PREDICT POOR SURVIVAL

[1,2]Hanna Kosberg Bredin, [3,4]Jan-Inge Bjune, [1,2]Hege Berg, [1,2]Mari Kyllestø Halle, [3,4]Gunnar Mellgren, [1,2]Jone Trovik, [1,2]Camilla Krakstad, [1,2]Erling Andre Hoivik. [1]*Department of Clinical Science, University of Bergen, Bergen, Norway*; [2]*Department of Obstetrics and Gynecology, Haukeland University Hospital, Bergen, Norway*; [3]*Hormone Laboratory, Department of Biochemistry and Pharmacology, Haukeland University Hospital, Bergen, Norway*; [4]*Mohn Nutrition Research Laboratory, Department of Clinical Science, University of Bergen, Bergen, Norway*

10.1136/ijgc-2022-ESGO.871

Introduction/Background *NRIP1*, encoding an obligate cofactor to the estrogen receptor alpha (ERα), is a significantly mutated gene in endometrial cancer (EC) with possible implications on hormone signaling and cancer development. We aimed at determining the prognostic impact of *NRIP1* mutations and mRNA expression in patients with ERα-positive EC, and functionally test patient-observed mutations *in vitro* on ERα-dependent transcriptional activity.

Methodology Sanger sequencing of recurring *NRIP1* frameshift mutations was performed on 242 EC patients enriched for ERα-positive tumors (endometrioid histology). Transcriptional profiles of 305 patients, in part overlapping with the sequenced samples, were used to investigate differentially expressed genes between *NRIP1* mutated/non-mutated tumors, and to determine the relation of *NRIP1* mutation status with expression and patient survival. A dual-luciferase reporter assay was used to uncover the effect of NRIP1-mutants on ERα-regulated gene transcription using COS-1 cells.

Results Hotspot *NRIP1* mutations were identified in 5.4% of the samples, and associated with high FIGO-stage, deep myometrial infiltration, and positive lymph-node status. However, there was no significant difference in disease-specific survival between patients with mutated and wildtype *NRIP1*, and mutation status did not associate with *NRIP1* expression levels. Interestingly, reporter assays showed that the repressive effect of wildtype NRIP1 was significantly abolished with NRIP1 mutants. Further, low *NRIP1* expression levels were significantly associated with decreased disease-specific survival, high grade, negative ERα status and low BMI. Gene Set Enrichment Analysis revealed an increase in gene sets related to proliferation in *NRIP1* mutated tumors.

Conclusion The relatively low mutation rate hampers a firm conclusion on the prognostic value of *NRIP1* frameshift mutations in endometrioid EC. However, low *NRIP1* expression may be a marker of poor prognosis. Our functional investigations demonstrates that frameshift mutated *NRIP1*, compared to wildtype *NRIP1*, have a significantly reduced corepressor effect on ERα-transcriptional activity, suggesting a possible effect on estrogen signaling.

2022-RA-807-ESGO MLH1 PROMOTER METHYLATION ANALYSIS IN PATIENTS WITH ENDOMETRIAL CANCER STAGE I-II

[1]Irina Tripac, [2]Valentina Stratan, [2]Valeriu Tutuianu, [2]Victor Sitnic, [3]David Faraggi, [4]Jean Calleja Agius. [1]*Gynaecology, Institute of Oncology, Chisinau, Moldova, Republic of*; [2]*Laboratory of Immunology and Molecular Genetics, Institute of Oncology, Chisinau, Moldova, Republic of*; [3]*University of Haifa, Haifa, Israel*; [4]*Department of Anatomy, Faculty of Medicine and Surgery, University of Malta, Malta, Malta*

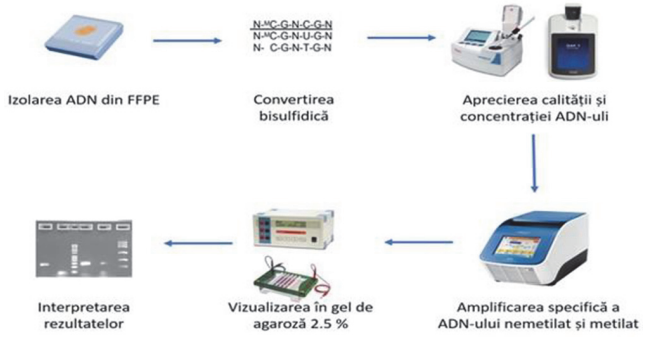
10.1136/ijgc-2022-ESGO.872

Introduction/Background The study included 50 patients diagnosed with endometrial cancer (EC) stage I-II. The age of these patients, on average, was 49.1 ± 12.1 years and ranged from 54 to 86 years.

Methodology The tumor DNA was extracted from mapped formalin-fixed, paraffin-embedded tissue sections to provide tumor samples for the assays (figure 1).

The methylation status of the MLH1 gene was determined using the Methylation Specific Polymerase Chain Reaction (MS-PCR) method and specific primers for both unmethylated and methylated fragments.

Results The frequency of MLH1 promoter methylation was 20.0% and was determined in 10 patients. The frequency of tumors with MLH1 promoter methylation increases during menopause, reaching 30.0% at the age of 50–59 years and 50, 0% of cases at 60–69 years and decreases in the age periods 70–79 years, reaching 20.0%.The analysis of the obtained results showed that in patients with EC, the presence of MLH1 epimutation was significantly higher in stage I of the disease.



Abstract 2022-RA-807-ESGO Figure 1 Methylation chain-specific polymerization reation workflow

Abstract 2022-RA-807-ESGO Table 1 MLH1 dependence on stage of the disease in patients with endometrial cancer in stages I-II

FIGO stage	MLH1 promoter methylation				P
	Negativ		Positive		
	Abs.	%	Abs.	%	
I	34	68,0	8	22,0	χ2=0,001; gl=1; p>0,05
II	6	8,1	2	4	

The presence of MLH1 epimutation was observed in 22.0% of patients with stage I EC and only in 2 stage II patients. The results of the analysis of overall survival in patients, according to the presence of MLH1 epimutation, showed that 71% of women with MLH1 epimutation and 92.5% without MLH1 epimutation survived at 3 years.