

**Objectives** There is no established screening strategy for Lynch syndrome (LS) in synchronous endometrial (EC) and ovarian cancers (OC). Most centers use mismatch repair (MMR) immunohistochemistry (IHC) on endometrium only. We aim to examine the concordance in MMR expression between tumor sites in synchronous EC/OC.

**Methods** Thirty women with newly diagnosed synchronous EC/OC were prospectively recruited from three cancer centers in Ontario, Canada. Tumor sites were assessed for MMR deficiency by IHC and MSI testing. All women underwent germline testing for MMR mutations.

**Results** Out of 30 cases, twelve cases (40%) were either MMRd or MSI-H, with 5 (17%) confirmed to have a pathogenic germline mutation: 3 MSH6, 1 MLH1 and 1 PMS2. MMR testing by IHC took place in both ovary and endometrium in 27 cases and results were discordant between two sites in 2 cases (7%). MSI testing in both sites took place in 24 cases, and results were discordant in 2 cases (8%). Out of the 5 cases with confirmed LS, performing IHC alone on endometrium would have missed the diagnosis in 1 case, and performing MSI testing alone on endometrium would have missed the diagnosis in 3 cases, which all had a MSH6 mutation. One case of LS was missed by both IHC and MSI testing.

**Conclusions** The incidence of LS was high in women with synchronous EC/OC (17%). Given the discordance in IHC and MSI results at the two tumor sites, consideration should be given to direct germline testing in all cases of synchronous EC/OC.

IGCS20\_1277

265 **IMPACT OF MISMATCH REPAIR PROTEIN AND PD-L1 EXPRESSION FOR THERAPEUTIC STRATIFICATION IN JAPANESE OVARIAN CLEAR CELL CARCINOMA**

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10.1136/ijgc-2020-IGCS.227

**Objective** Ovarian clear cell carcinoma (OCCC) is a rare type of epithelial ovarian cancer that behaves comparable to a distinct entity. Novel genomic and immunological profiling-based strategies targeting OCCC remain unavailable. ARID1A, which is one of the most frequently mutated genes in OCCC, could be a druggable target as well as a regulator of mismatch repair (MMR). Most of the mutated neoantigens in MMR-deficient cancers sensitize them to immune checkpoint blockade. However, the role and frequency of MMR deficiency in OCCC are still poorly understood. We aimed to evaluate the abnormal expression frequency of MMR and PD-L1 proteins in OCCC for identifying the effective OCCC population with immune checkpoint blockade.

**Methods** The study cohort comprised 113 patients with OCCC treated at a single institution. Protein expression levels in ARID1A, MLH1, PMS2, MSH2, MSH6, and PD-L1 were evaluated by immunohistochemistry (IHC). We investigated the correlations between immunoreactivity for MMR/PD-L1 and clinicopathological parameters including ARID1A status.

**Results** MMR proteins disappeared in two cases (1.8%), specifically those who had synchronous double cancer with endometrial carcinoma and a family history of Lynch syndrome-related tumor. PD-L1 expression was diffused in 17 cases (15.0%). The diffused PD-L1 expression was significantly associated with ARID1A expression loss (p = 0.003), but no other correlations existed between PD-L1 expression and clinical parameter.

**Conclusions** Although only few Japanese OCCC cases showed MMR deficiency as evaluated by IHC, immune checkpoint signals were activated even in MMR-intact OCCC, possibly through ARID1A interaction.

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266 **INTRA-EPITHELIAL SPREADING OF CERVICAL SQUAMOUS CELL CARCINOMA TO THE UPPER GENITAL TRACT**

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10.1136/ijgc-2020-IGCS.228

**Abstract 266 Table 1** Clinical characteristics of cervical squamous cell carcinoma involving the upper genital tract

Case No.	Age	Menopause	Clinical presentation	TCT	Cervix tumor size (cm)	Clinical Stage	Treatment	Post operation treatment	Follow up (months)	Prognosis	Uterine apoplexis	Pre operation condition
1	72	Y	bleeding	NA	NED	IA1	TAH+BSO	NO	48	AOD	Y	
2	53	Y	NA	HSIL	NED	IA2	TAH+BSO	R	96	AOD	N	
3	41	N	bleeding	NA	2	IB1	TAH+BSO+LN	C+R	39	AOD	N	chemotherapy
4	63	Y	NA	NA	1	IB1	TAH+BSO+LN	NA	NA	AOD	NA	NA
5	59	Y	discharge	HSIL	2.2	IB1	TAH+BSO+LN	C+R	72	AOD	N	
6	60	Y	bleeding	NA	3.5	IB1	TAH+BSO+LN	C+R	75	AOD	Y	thyroid hypo function
7	59	Y	bleeding	HSIL	1.5	IB1	TAH+BSO+LN	C+R	75	AOD	N	PTC
8	48	N	bleeding	HSIL	2.5	IIA	TAH+BSO+LN	C+R	86	AOD	N	
9	55	Y	bleeding	ASC-H	NA	IIA	TAH+BSO+LN	C+R	22	DOD	N	chemotherapy
10	52	Y	bleeding	NA	5	IIIB	TAH+BSO+LN	C+R	71	AOD	Y	immune deficiency
11	46	N	bleeding	ASC-H	4	IIIB	TAH+BSO+LN	C+R	62	AOD	N	chemotherapy
12	56	Y	Bleeding	NEG	1.5	IB1	TAH+BSO+LN	C+R	1	AOD	Y	N
13	54	Y	bleeding	HSIL	1	IB1	TAH+BSO+LN	C+R	12	AOD	N	
14	58	Y	bleeding	NA	NA	IA1	TAH+BSO	C+R	20	AOD	N	
15	50	Y	NO	HSIL	NED	0	TAH+BSO	C+R	54	AOD	Y	

NA, not available; HSIL, high-grade squamous intraepithelial lesion; ASC-H, atypical squamous cells—cannot exclude high grade squamous intraepithelial lesion; TAH, total pelvic hysterectomy; BSO, bilateral salpingoophorectomy; LN, lymphoadectomy; C, chemotherapy; R, radiation therapy; AOD, alive without disease; AWD, alive with disease; PTC, papillary thyroid carcinoma.