

the calculated predictive probability values were significantly different between the LNM-positive and -negative groups ( $P = 1.39 \times 10^{-10}$ ), and high diagnostic accuracy of 83.6% area under the curve (AUC) was obtained. The LNM diagnosis requires essentially minimize the time difference between the diagnosis and hysterectomy. Therefore, reverse transcription-polymerase chain reaction enabled quantification from RNA in one step within 30 min, for intraoperative diagnosis.

**Conclusion** This diagnostic method uses rapid nucleic acid amplification for intraoperative quantification of biomarkers in the primary tissue. Furthermore, the predictive model combined with various clinical variables can be used to discriminate LNM with high accuracy and facilitate individualization of the surgical treatment.

2022-RA-809-ESGO

#### UNDERLYING CAUSES AND PROGNOSIS OF MISMATCH REPAIR DEFICIENCY IN ENDOMETRIAL CANCER OTHER THAN *MLH1* PROMOTER HYPERMETHYLATION

<sup>1</sup>Merve Kaya, <sup>2</sup>Cathalijne Post, <sup>3</sup>Carli M Tops, <sup>4</sup>Ellen Stelloo, <sup>3</sup>Maartje Nielsen, <sup>5</sup>Melanie E Powell, <sup>6</sup>Alexandra Leary, <sup>7</sup>Linda R Mileskin, <sup>8</sup>Paul Bessette, <sup>2</sup>Stephanie M de Boer, <sup>9</sup>Ina M Jürgenliemk-Schulz, <sup>10</sup>Ludy Lutgens, <sup>11</sup>Jan J Jobsen, <sup>12</sup>Elzbieta M van der Steen-Banasik, <sup>2</sup>Remi A Nout, <sup>2</sup>Nanda Horeweg, <sup>4</sup>Tom van Wezel, <sup>4</sup>Vincent Smit, <sup>2</sup>Carien L Creutzberg, <sup>4</sup>Tjalling Bosse. <sup>1</sup>Department of Medical Oncology, Leiden University Medical Center, Leiden, Netherlands; <sup>2</sup>Department of Radiation Oncology, Leiden University Medical Center, Leiden, Netherlands; <sup>3</sup>Department of Clinical Genetics, Leiden University Medical Center, Leiden, Netherlands; <sup>4</sup>Department of Pathology, Leiden University Medical Center, Leiden, Netherlands; <sup>5</sup>Department of Clinical Oncology, Barts Health NHS Trust, London, UK; <sup>6</sup>Department of Medical Oncology, Gustave Roussy, Villejuif, France; <sup>7</sup>Department of Medical Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia; <sup>8</sup>Department of Obstetrics and Gynaecology, University of Sherbrooke, Sherbrooke, QC, Canada; <sup>9</sup>Department of Radiation Oncology, University Medical Center Utrecht, Utrecht, Netherlands; <sup>10</sup>Department of Radiation Oncology, MAASTRO Clinic, Maastricht, Netherlands; <sup>11</sup>Department of Radiation Oncology, Medical Spectrum Twente, Enschede, Netherlands; <sup>12</sup>Department of Radiation Oncology, Radiotherapy Group, Arnhem, Netherlands

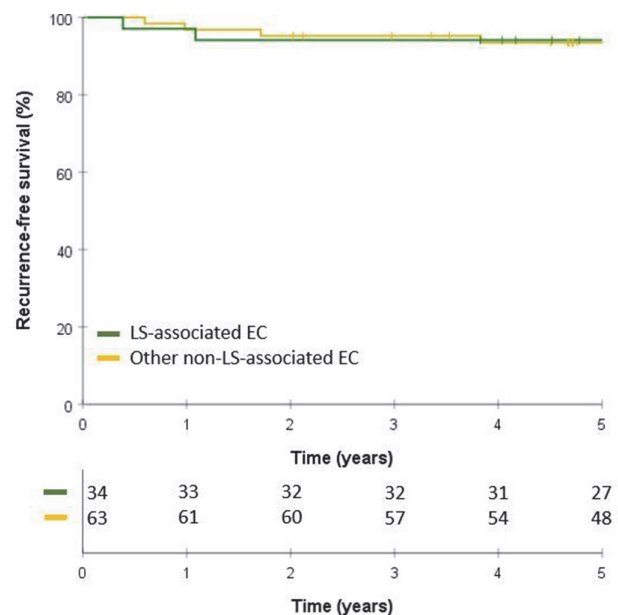
10.1136/ijgc-2022-ESGO.244

**Introduction/Background** The vast majority of mismatch repair-deficient (MMRd) endometrial carcinomas (EC) are due *MLH1* promoter hypermethylation. Here, we aimed to investigate the prevalence, prognosis and underlying causes (including Lynch syndrome (LS)) of MMRd EC other than *MLH1* promoter hypermethylation.

**Methodology** From the 409 MMRd ECs that were identified by MMR-immunohistochemistry (IHC) in the PORTEC-1,-2 and -3 trials, 97 cases did not have *MLH1* promoter hypermethylation. These 97 cases were analyzed by matched tumor-normal tissue targeted next-generation sequencing (NGS) for the presence of MMR and *POLE* mutations (class 4/5 variants). Furthermore, microsatellite instability (MSI) testing was performed. Differences in 5-year recurrence-free survival (RFS) were analysed using the Kaplan-Meier method and log-rank test. On a subset of cases NGS is pending and results will be added for the meeting.

**Results** In 34 cases (35%) a germline MMR mutation (LS-associated) was identified of which 8 (24%) had a second somatic hit. Upon excluding LS-associated ECs, a somatic alteration in MMR genes was observed in 52% (n=33), including double somatic hits in 35% (n=22). In the remaining 48% of cases (n=30) no MMR mutation was found of which the majority (n=22) was confirmed MSI. Rereview of all (discrepant) MMR-IHC did not reveal misinterpretation of

MMRd status. Somatic *POLE* mutations were identified in 7/97 cases (7%). The 5-year RFS did not differ significantly between LS-associated and non-LS-associated MMRd EC (5-year RFS 94.1% [95% CI 86.5–100%] vs 93.5% [95% CI 87.5–99.9%], respectively;  $p=0.72$ ; figure 1).



**Abstract 2022-RA-809-ESGO Figure 1** Kaplan-Meier survival curves for recurrence-free survival for patients with LS-associated EC (germline mutation in MMR gene) and other non-LS-associated MMRd EC. All Cases with MMRd phenotype without *MLH1* promoter hypermethylation are included in this analysis, including cases with a concurrent *POLE* mutation (*POLE*mut-MMRd EC). *P* value reflect 2-sided log-rank test. Abbreviations: EC, endometrial cancer; LS, Lynch syndrome; MMR, mismatch repair; MMRd, mismatch repair-deficient;

**Conclusion** Identification of an underlying cause for unmethylated MMRd is feasible in the majority of EC cases applying matched tumor-normal tissue NGS. A significant proportion was confirmed to be LS-associated or sporadic MMRd, while only a small subset remained unresolved. Although this distinction did not carry prognostic relevance, identification of definitive sporadic causes may release patients and relatives from burdensome LS-surveillance.

2022-RA-815-ESGO

#### ENDOMETRIAL CANCER INCIDENCE IN PATIENTS WITH ATYPICAL ENDOMETRIAL HYPERPLASIA ACCORDING TO MODE OF MANAGEMENT

<sup>1,2</sup>Anas Barakat, <sup>1</sup>Aemn Ismail, <sup>1,2</sup>Supratik Chattopadhyay, <sup>1</sup>Quentin Davies. <sup>1</sup>Gynaecology Oncology Department, University Hospitals of Leicester NHS Trust, LEICESTER, UK; <sup>2</sup>Leicester Cancer Research Centre, University of Leicester, Leicester, UK

10.1136/ijgc-2022-ESGO.245

**Introduction/Background** It is well established that around one-third of patients with atypical Endometrial hyperplasia (AEH) develop endometrial cancer (EC). The aim of the study is to determine the incidence of EC in AEH patients in UHL and to explore the reasons why AEH patients opted for conservative management.