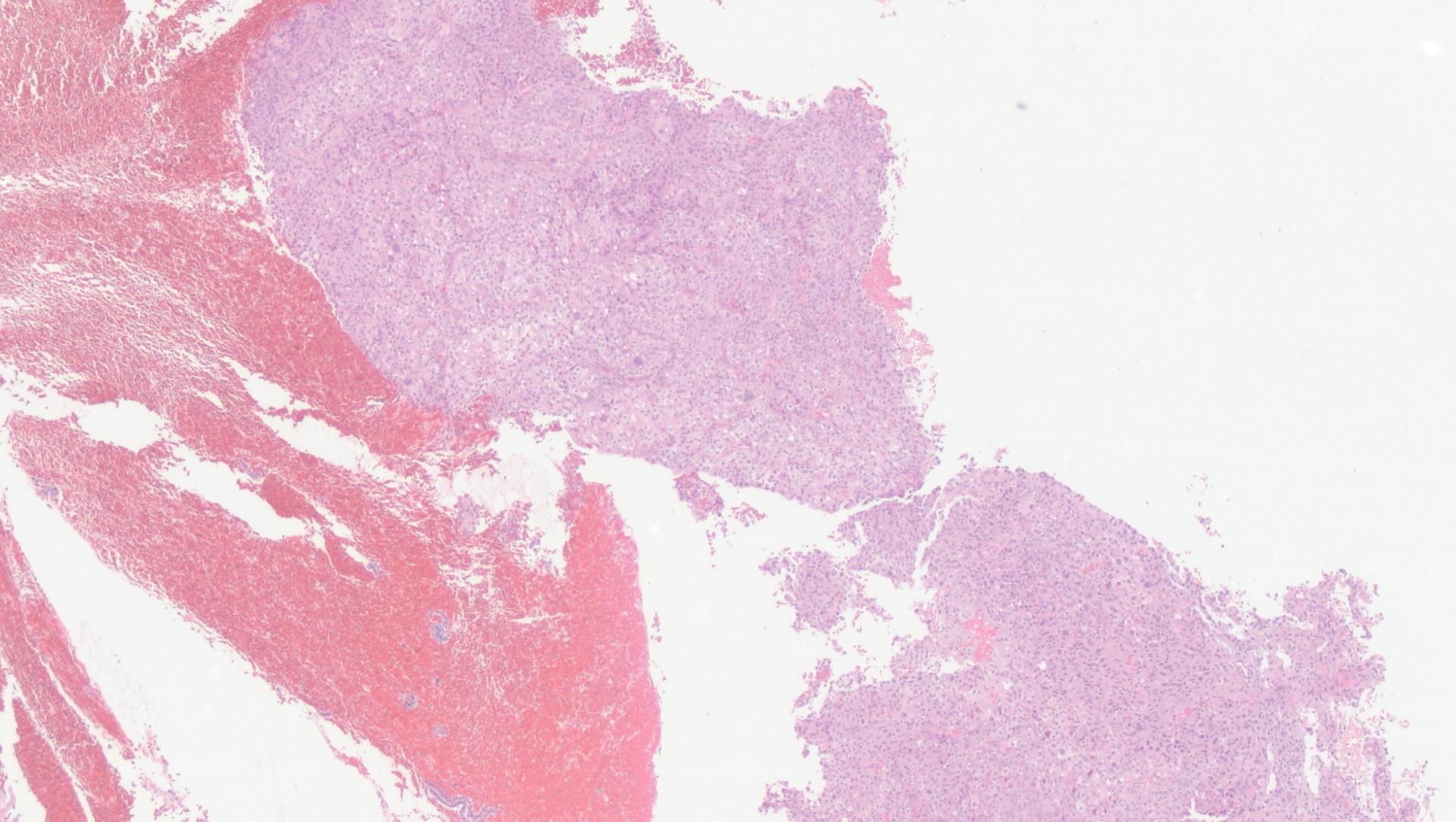


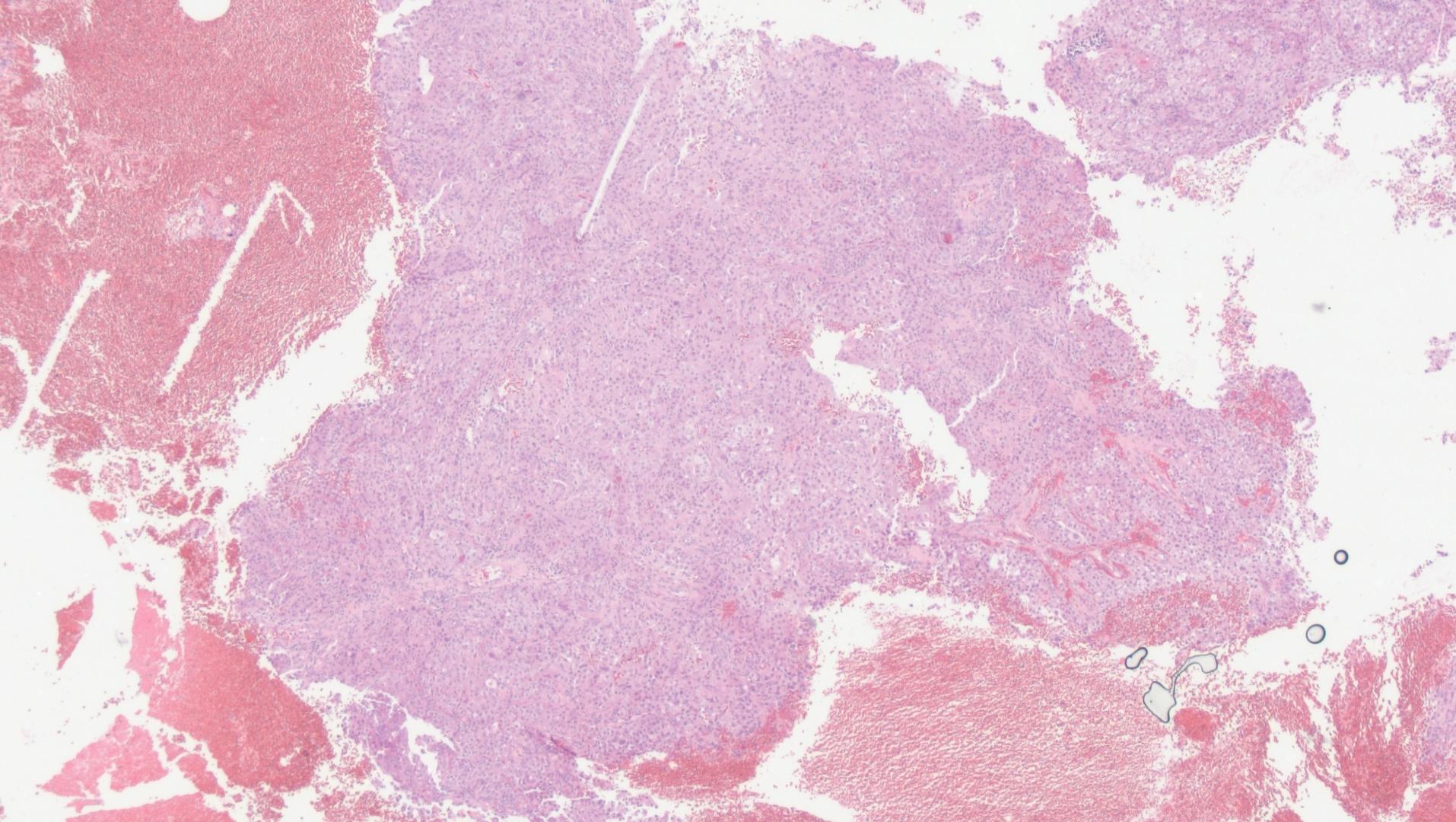
A CASE OF ENDOMETRIAL CANCER

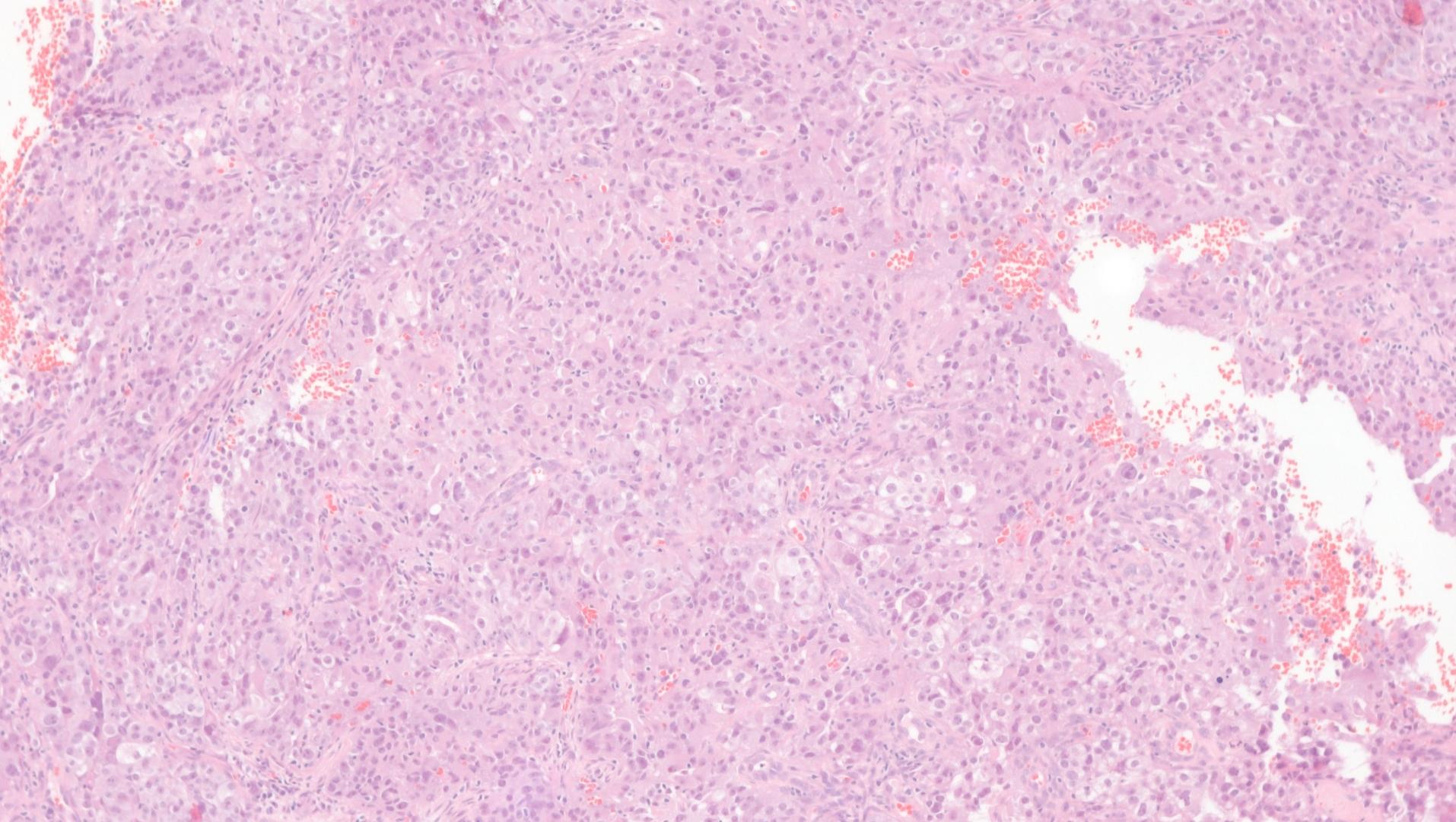
Blake Gilks

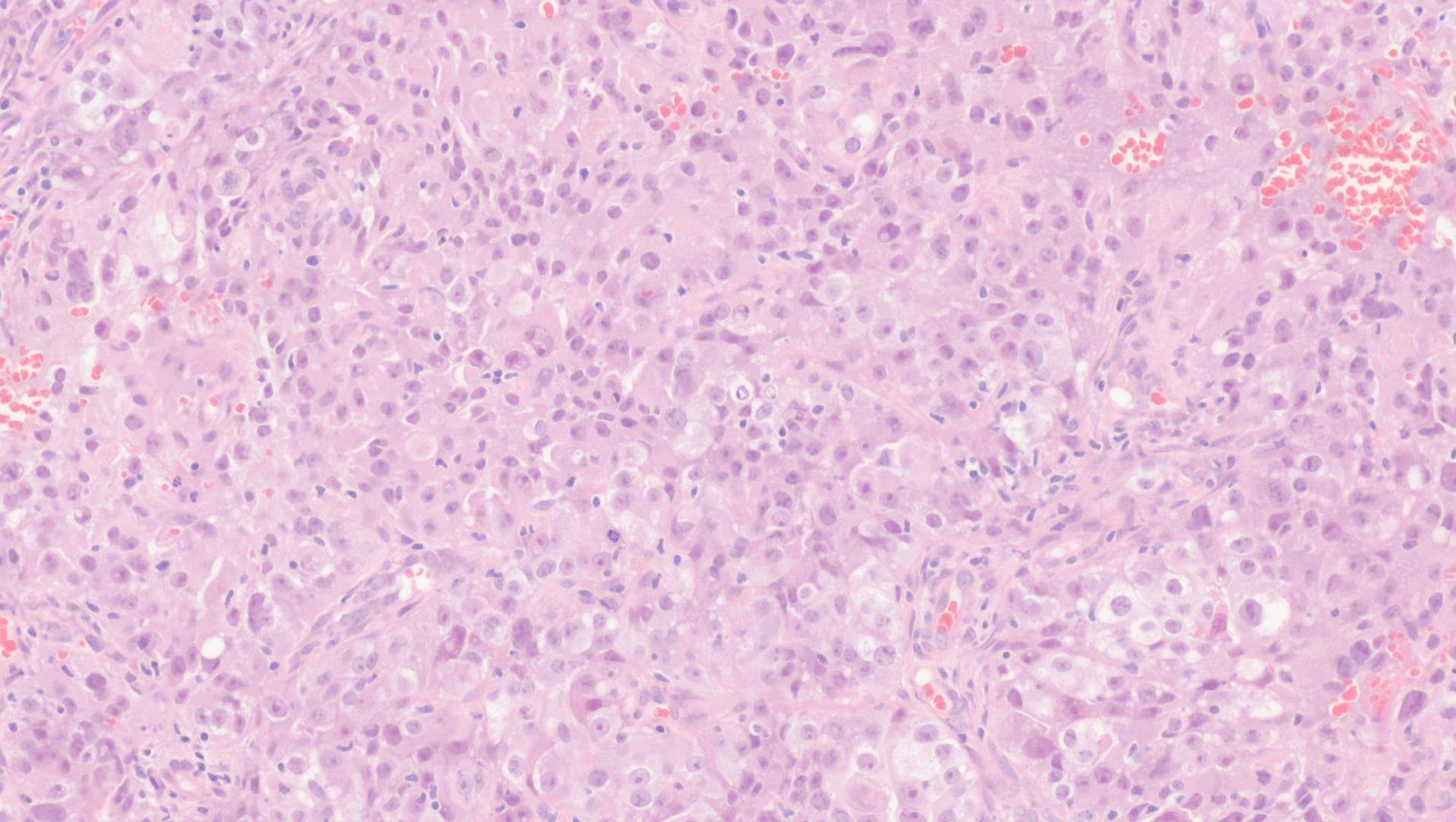
University of British Columbia, Vancouver, BC; ⁷BC Cancer Agency, Vancouver, BC

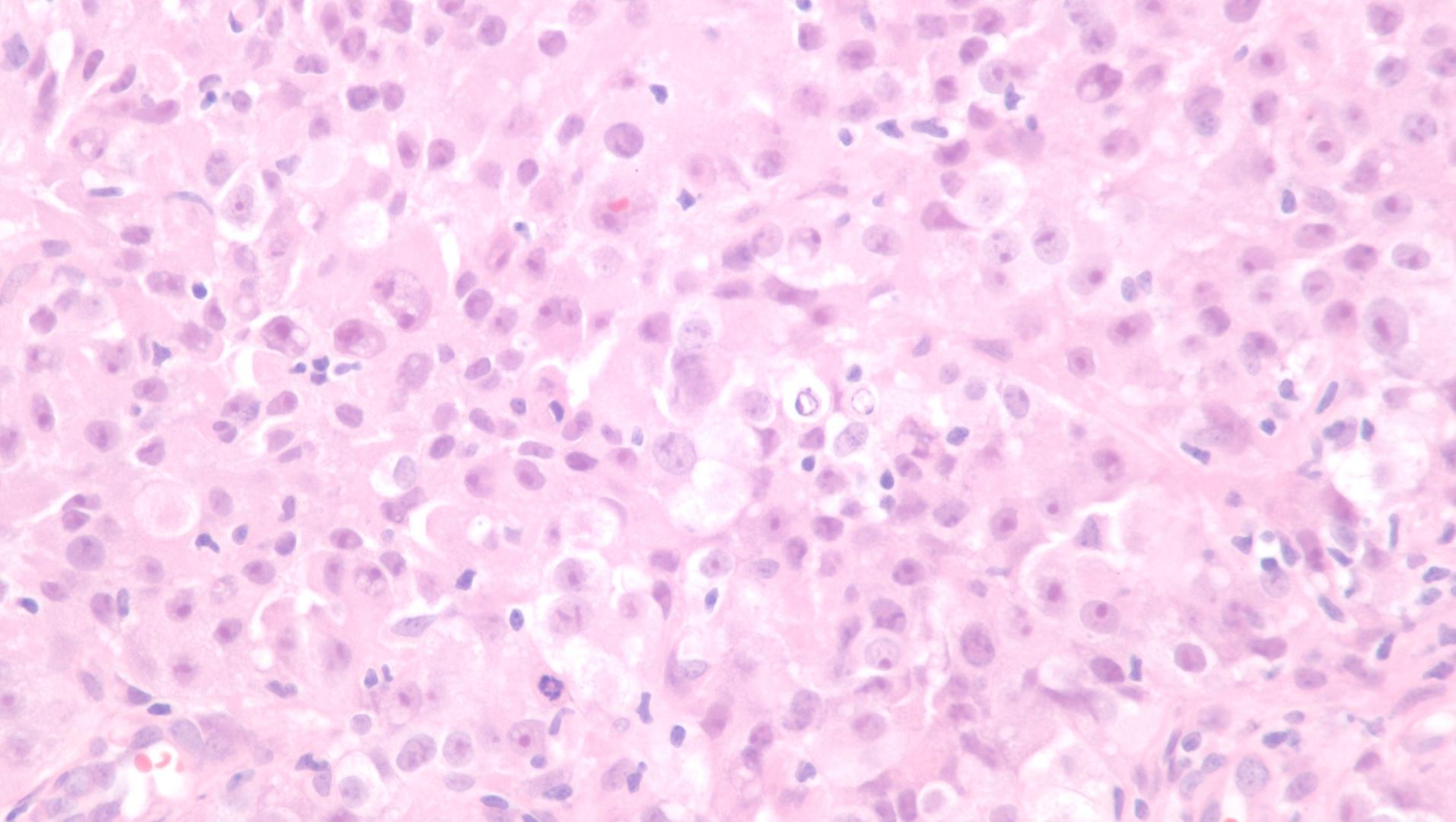
59 yo, PMB
endometrial biopsy performed











Diagnosis?

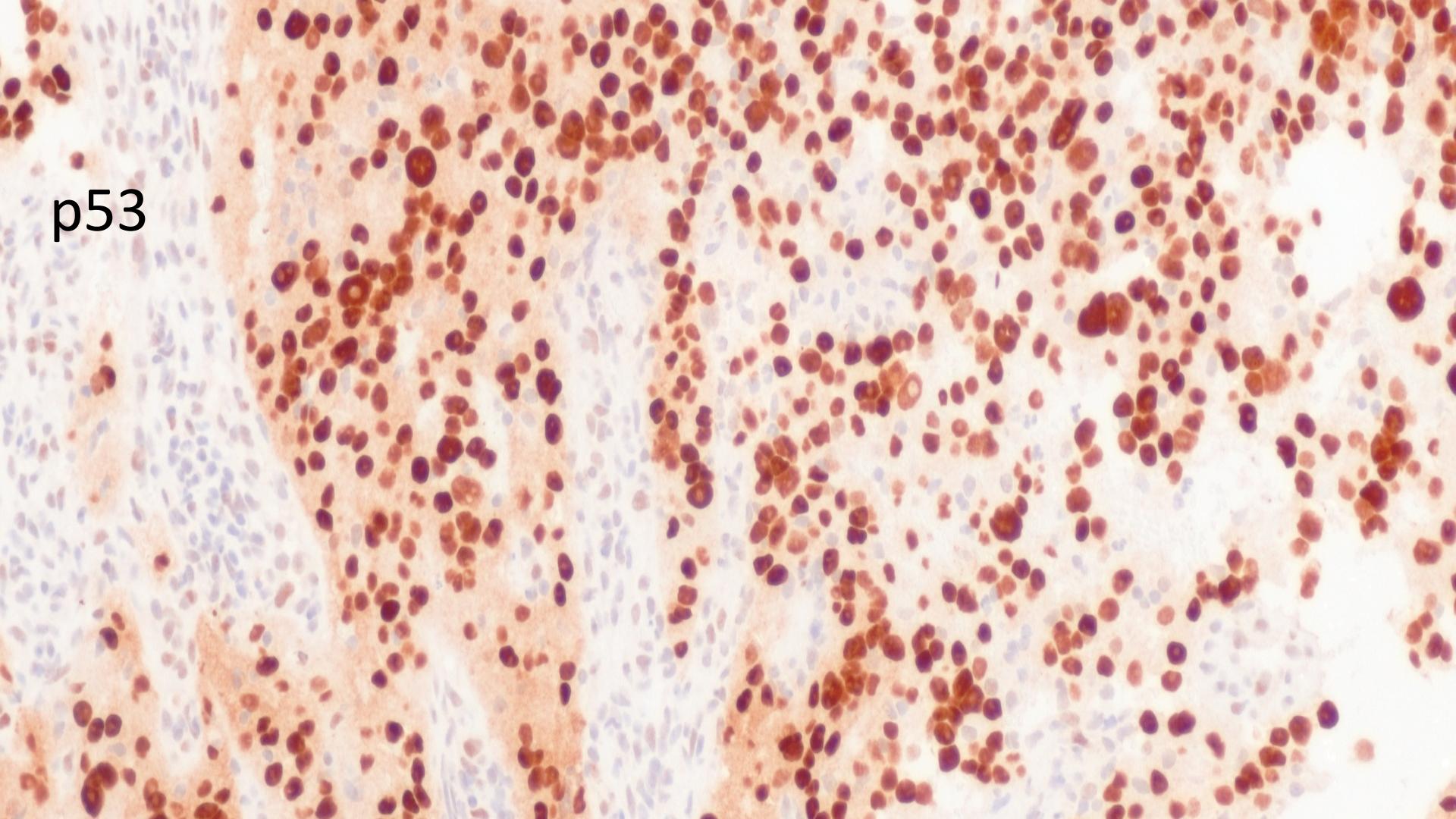
IHC

- p53abn (overexpressed)
- ER +

p53

This image shows immunohistochemical staining for the p53 protein. The staining is localized to the nuclei of individual cells, appearing as numerous small, dark reddish-brown dots. The background is a light blue-grey color, likely representing normal tissue or areas where the antibody did not bind. The overall pattern suggests a widespread presence of p53 protein across the field of view.

p53

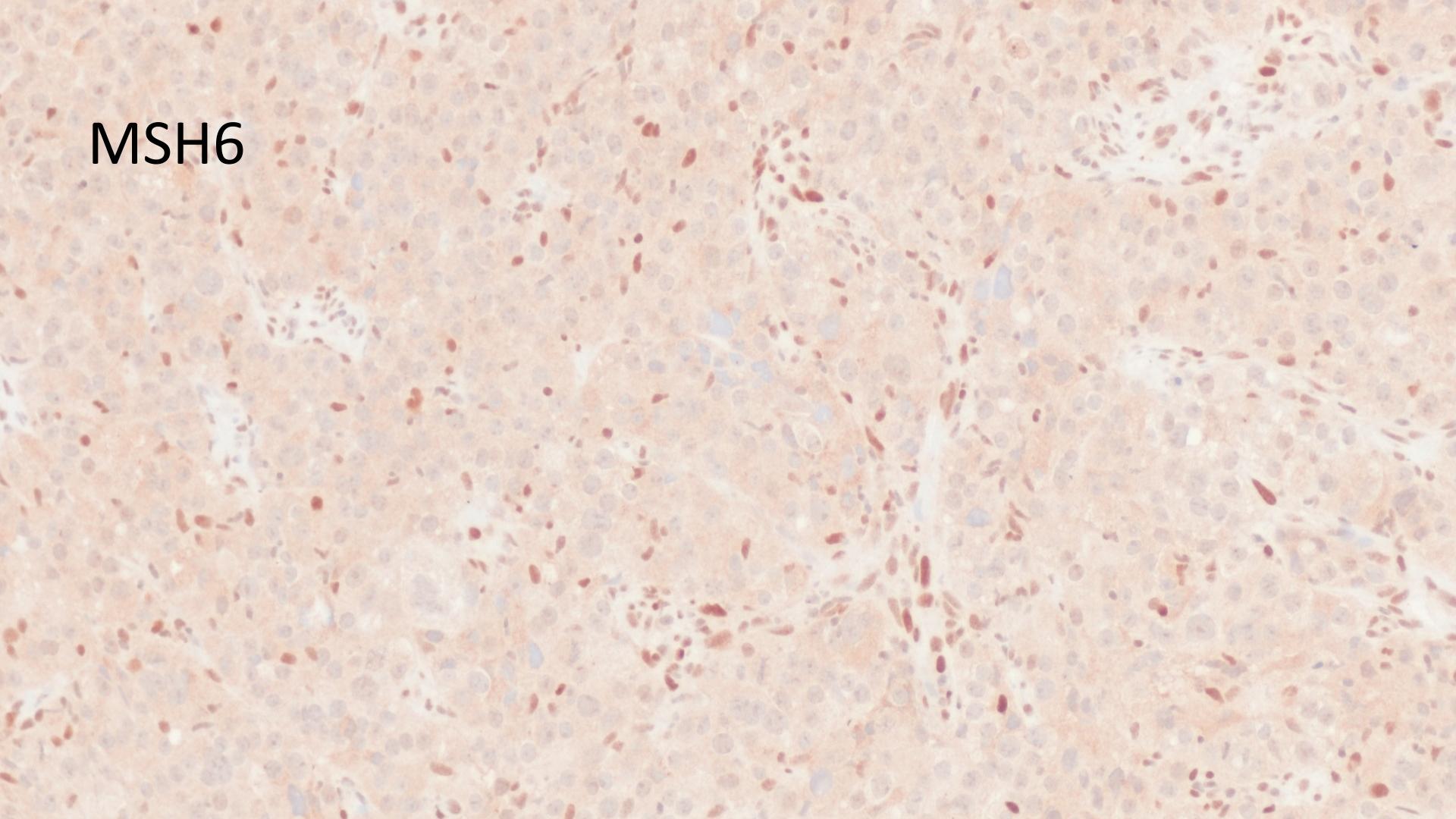


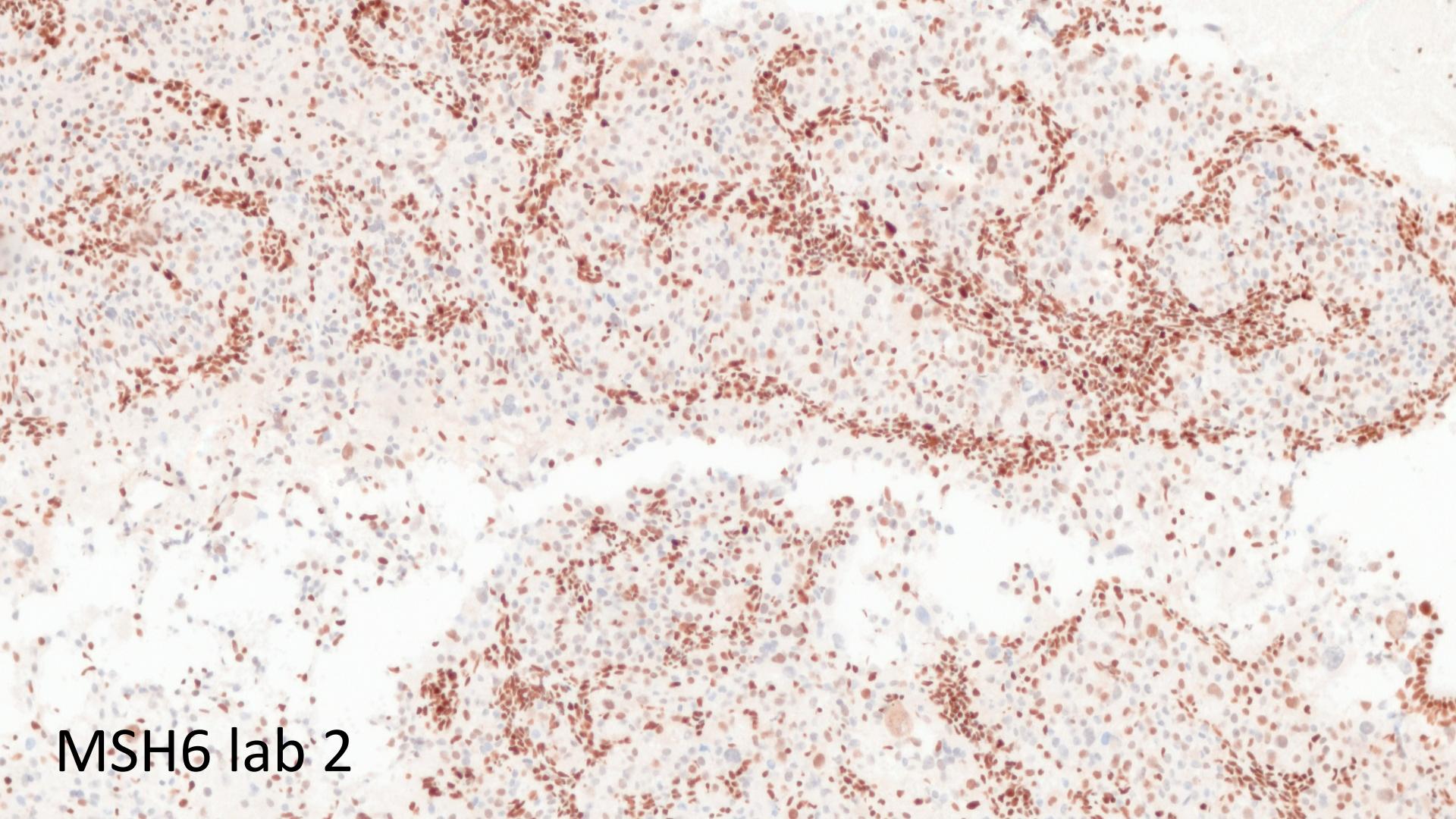
Diagnosis?

MSH6

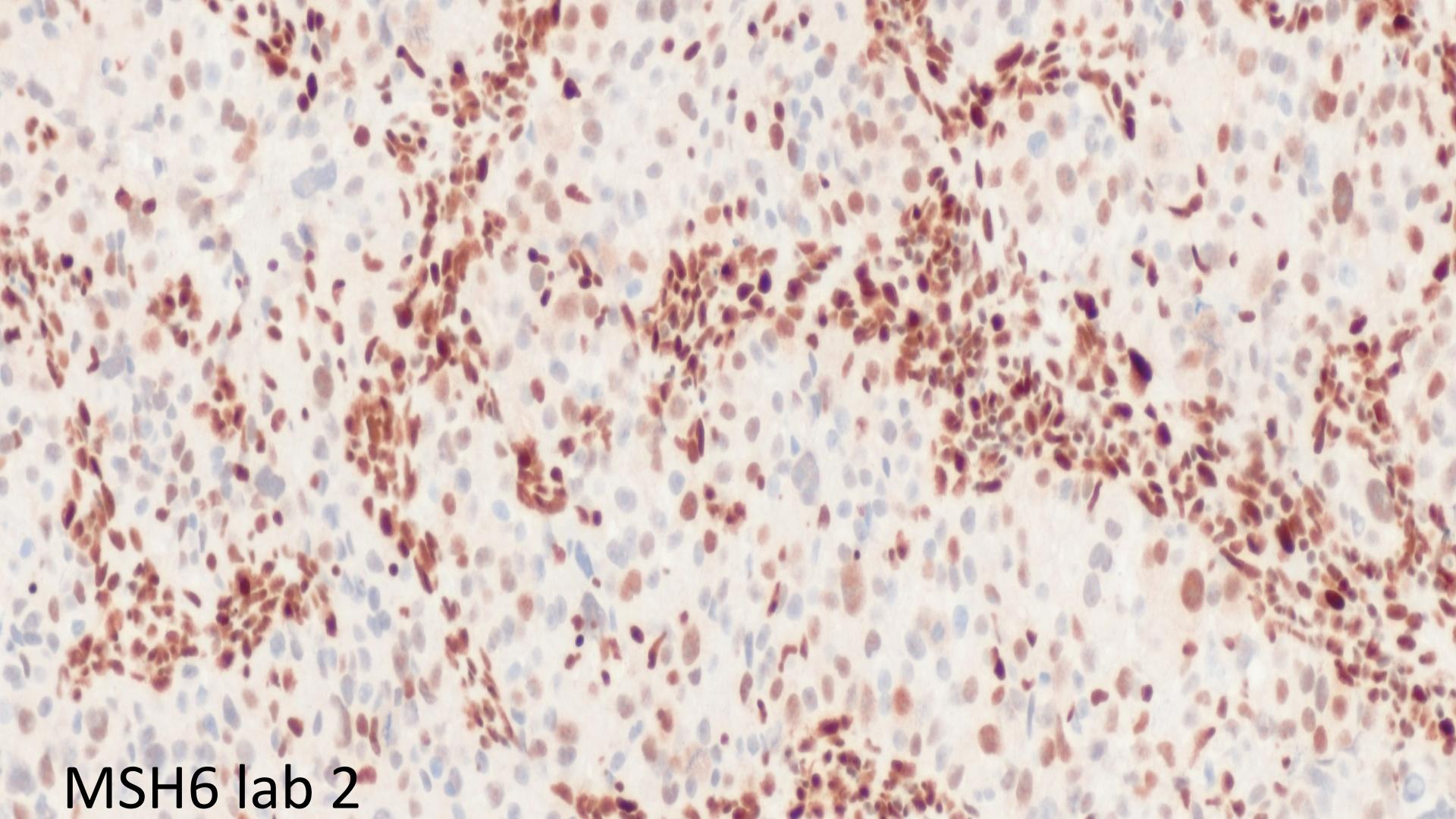


MSH6



A high-magnification micrograph showing numerous small, dark reddish-brown spots distributed throughout a light blue-grey background. These spots represent individual nuclei, many of which appear to contain a distinct red signal, likely indicating the presence of the MSH6 protein. The overall pattern is somewhat mottled and lacks a clear, organized structure.

MSH6 lab 2

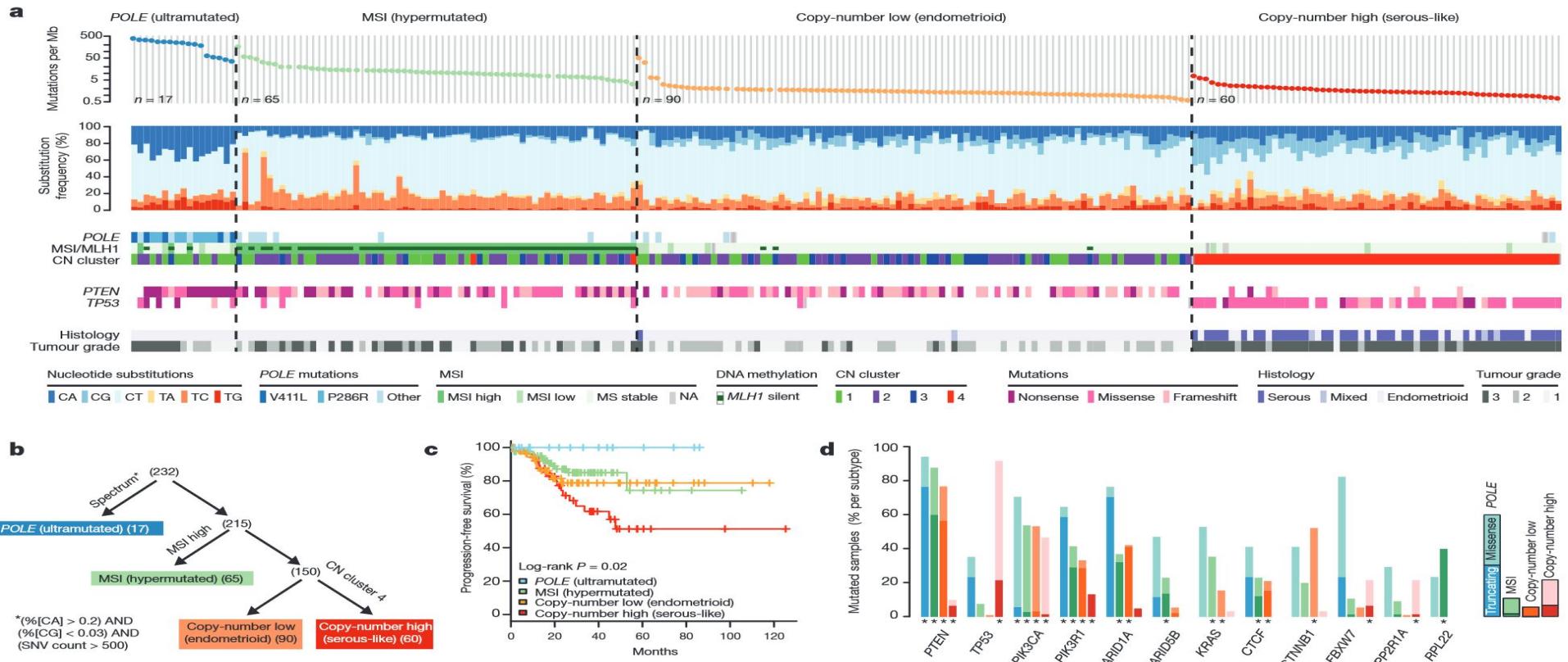
A high-magnification micrograph showing a dense cellular tissue section. The cells exhibit varying degrees of brownish-red staining, indicating the presence of the MSH6 protein. Some cells show strong nuclear staining, while others have more diffuse cytoplasmic or nuclear patterns. The overall distribution is somewhat heterogeneous.

MSH6 lab 2

Molecular subtypes of Endometrial Carcinoma

- There are four molecular subtypes:
 - MMRd (mismatch repair deficient, with hypermutated genomic architecture)
 - POLEmut (mutation in the exonuclease domain of POLE, with ultramutated genomic architecture)
 - p53abn (abnormal/mutant pattern p53 expression)
 - p53 wildtype (also referred to as No Specific Molecular Phenotype or NSMP: lacking any of the above abnormalities)

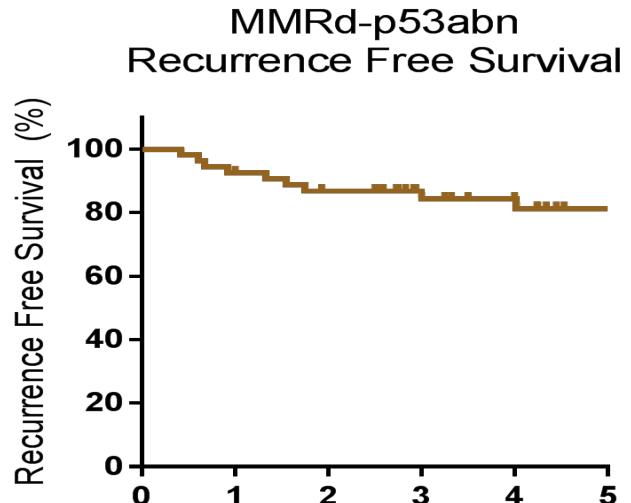
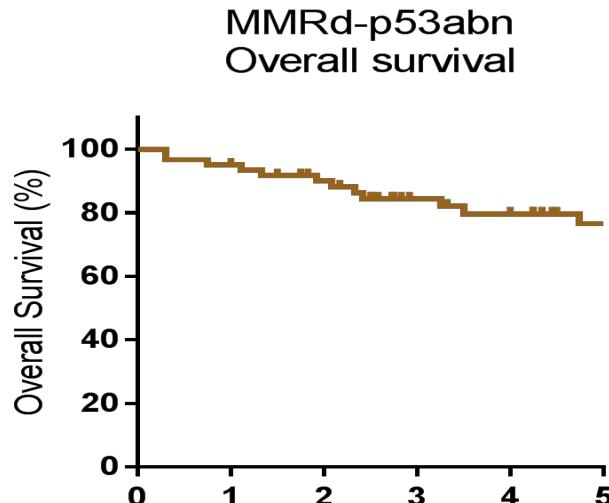
The Cancer Genome Atlas (TCGA): Endometrial Carcinoma



What to do when there is more than one molecular feature?? The clinical outcomes for patients with MMRd and p53abn is the same as for MMRd alone, and better than for patients with p53abn alone. Therefore, MMRd + p53abn is classified as MMRD!!!!

- Reference: **Clinicopathological and Molecular Characterisation of “Multiple Classifier” Endometrial Carcinomas**
- Alicia León-Castillo, Ester Gilvazquez, Remi Nout, Vincent T.H.B.M. Smit, Jessica N. McAlpine, Melissa McConechy, Stefan Kommooss, Sara Y. Brucker, Joseph W. Carlson, Elisabeth Epstein, Tilman T. Rau, Robert A. Soslow, Raji Ganesan, Xavier Matias-Guiu, Esther Oliva, Beth T. Harrison, David N Church, C. Blake Gilks, Tjalling Bosse.
- J Pathol, in press.

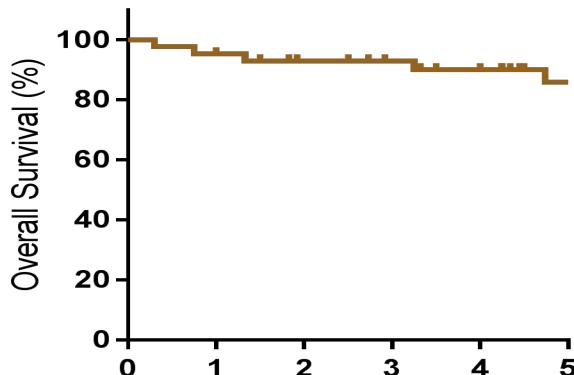
MMRd-p53abn EC: Survival analysis



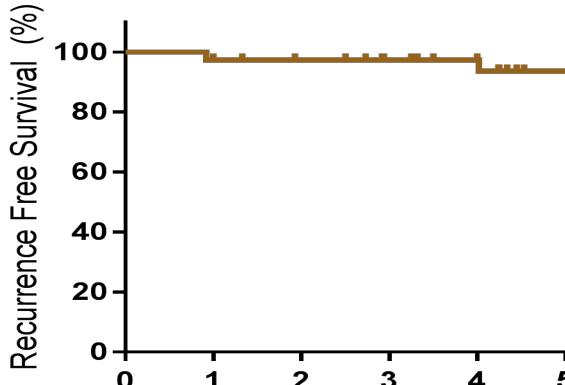
MMRd-p53abn EC have a 5-year RFS of 81% and OS of 77%

MMRd-p53abn EC: Survival analysis, Stage I

MMRd-p53abn
Overall Survival
Stage I



MMRd-p53abn
Recurrence Free Survival
Stage I



Stage I MMRd-p53abn EC have a 5-year RFS of 94% (n=39) and OS of 86% (n= 44).

Diagnosis

- MMRd Endometrial Carcinoma, grade 3/3

Learning Points

- Interpretation of p53 IHC in endometrial carcinoma requires knowledge of MMR status
- There are four types of EC: p53wt/NSMP (corresponding to classic Type I EC), p53abn (corresponding to classic Type II EC), MMRd and POLEmut