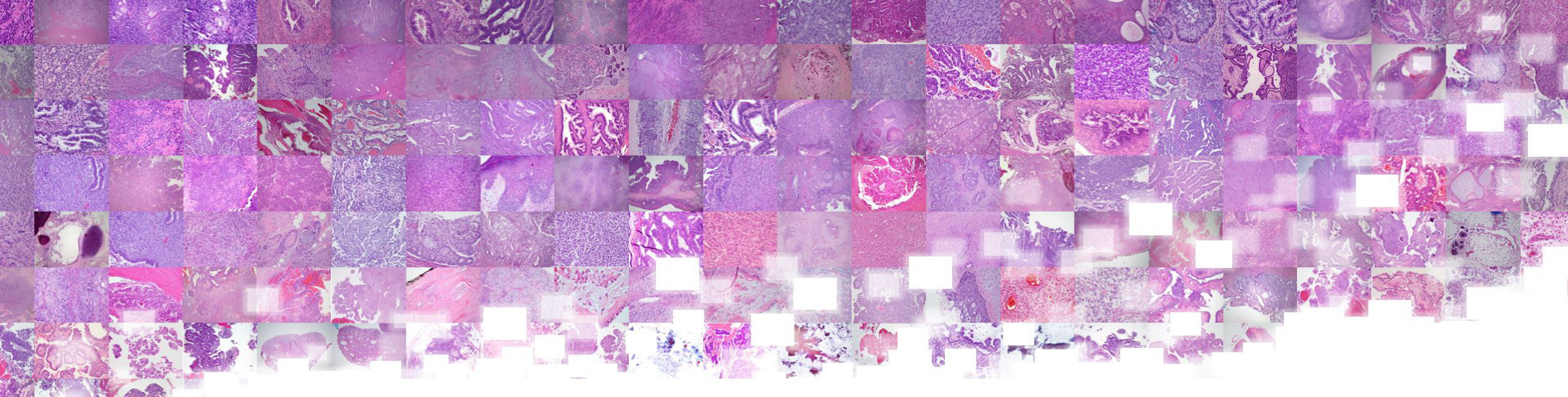


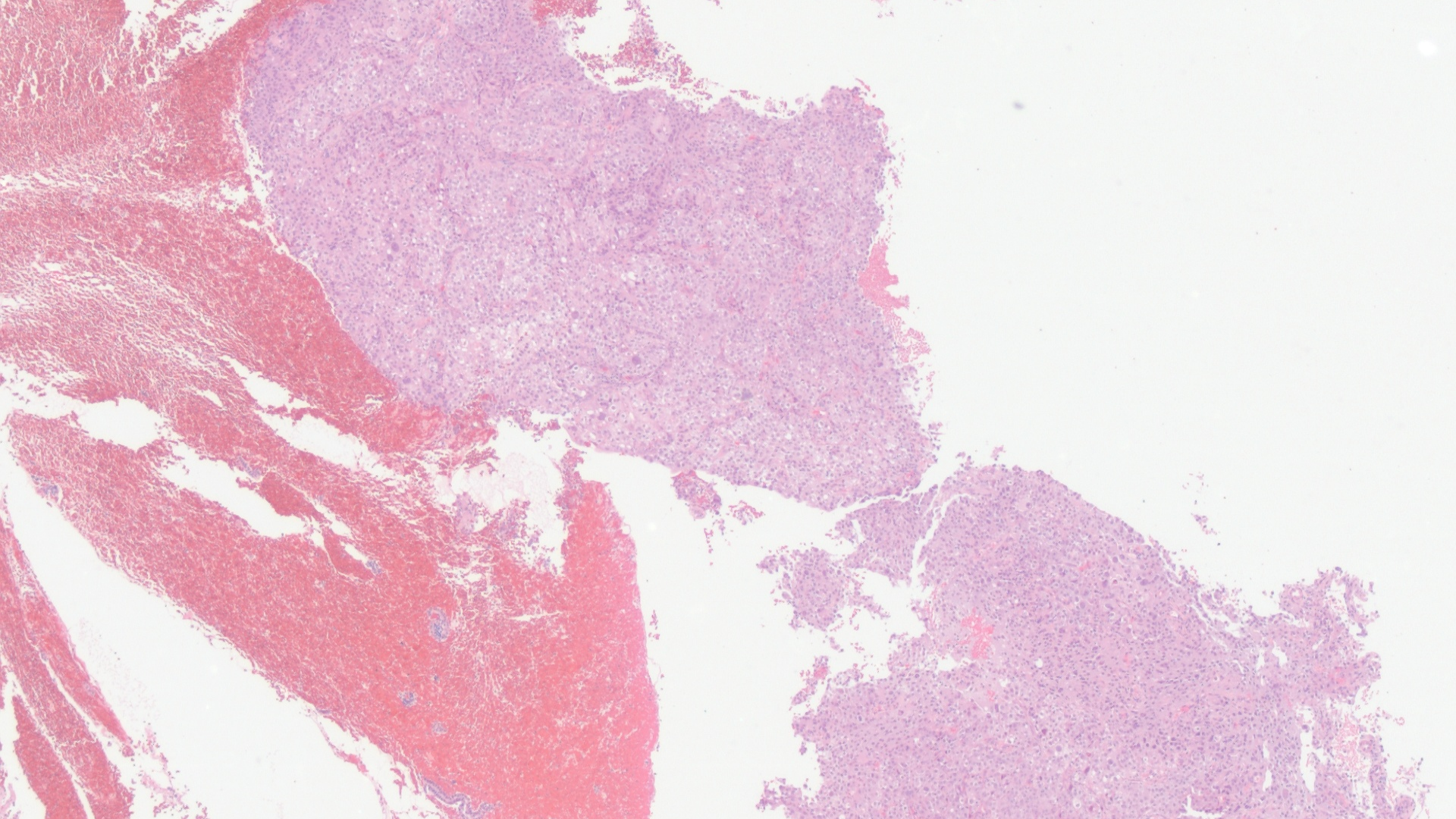


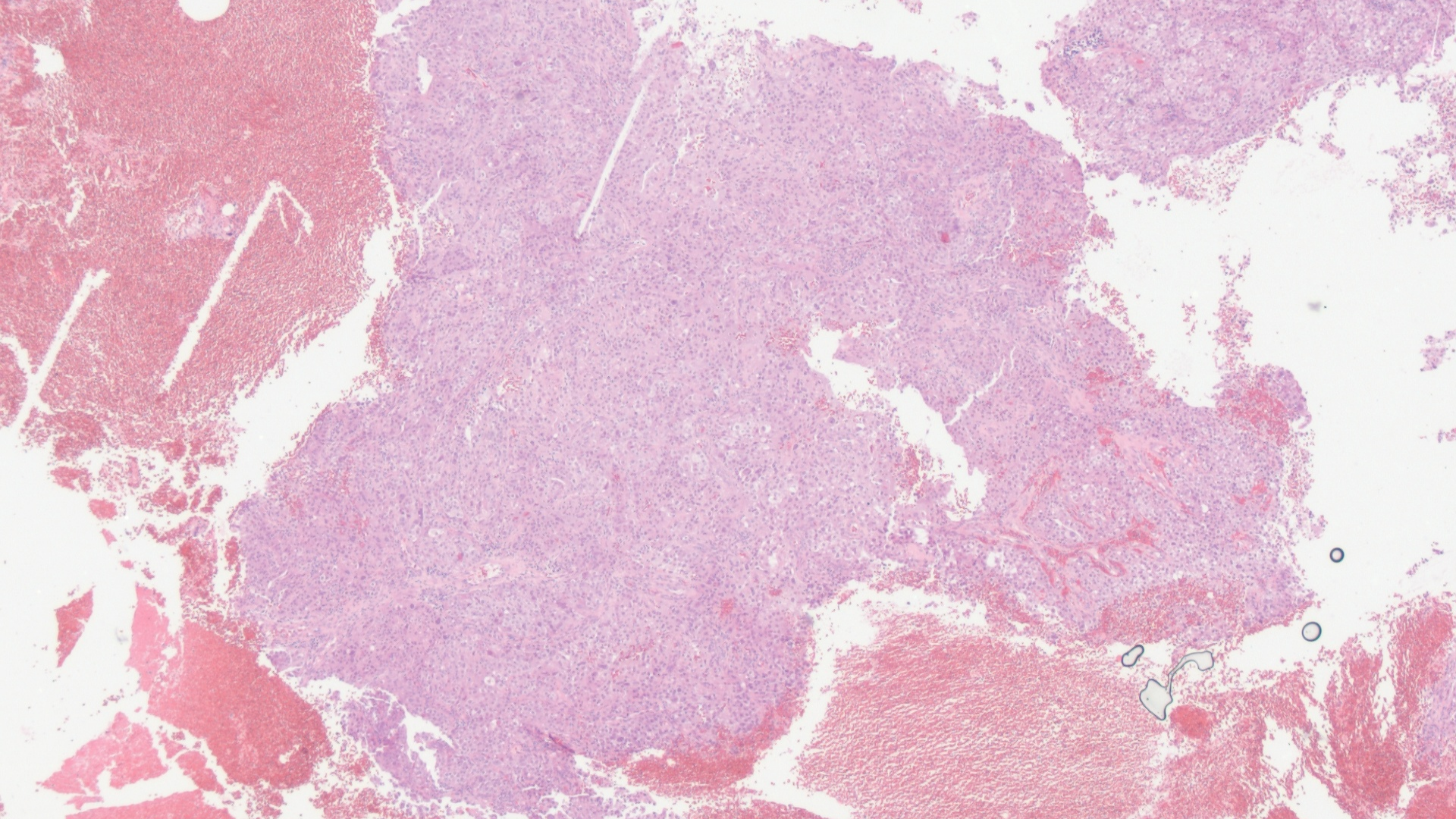
A CASE OF ENDOMETRIAL CANCER

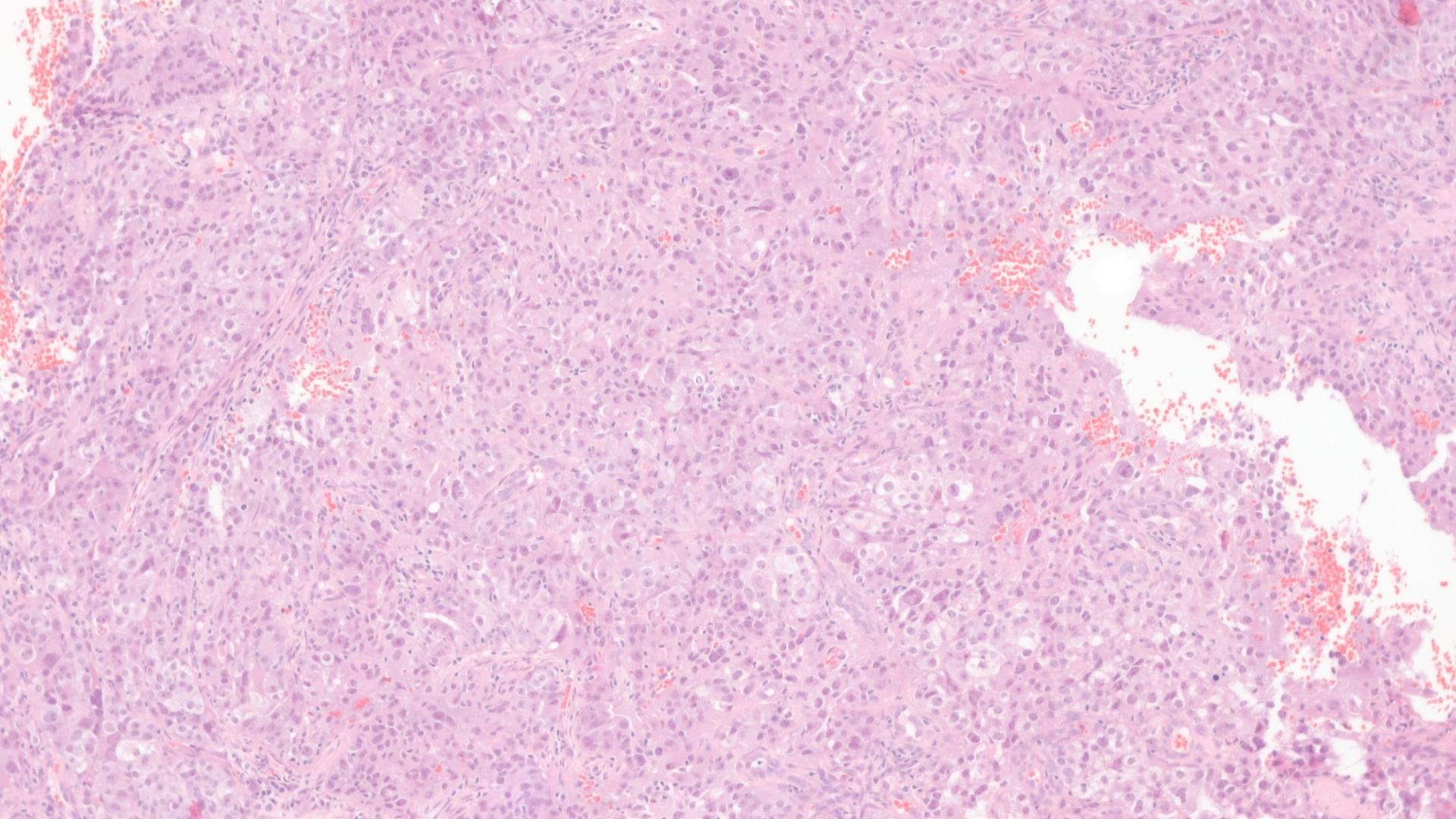
Blake Gilks

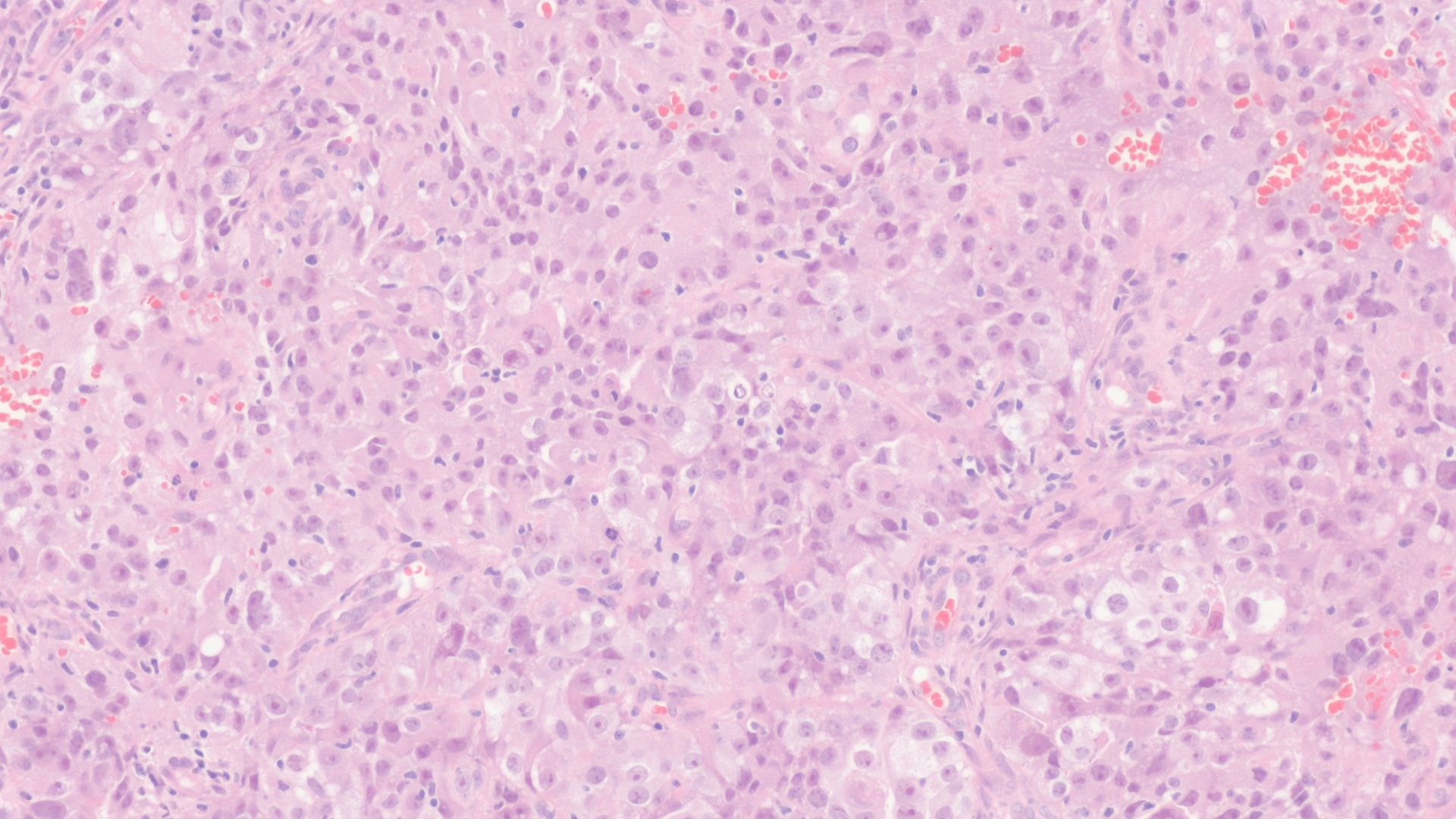
*University of British Columbia, Vancouver, BC; ⁷BC Cancer
Agency, Vancouver, BC*

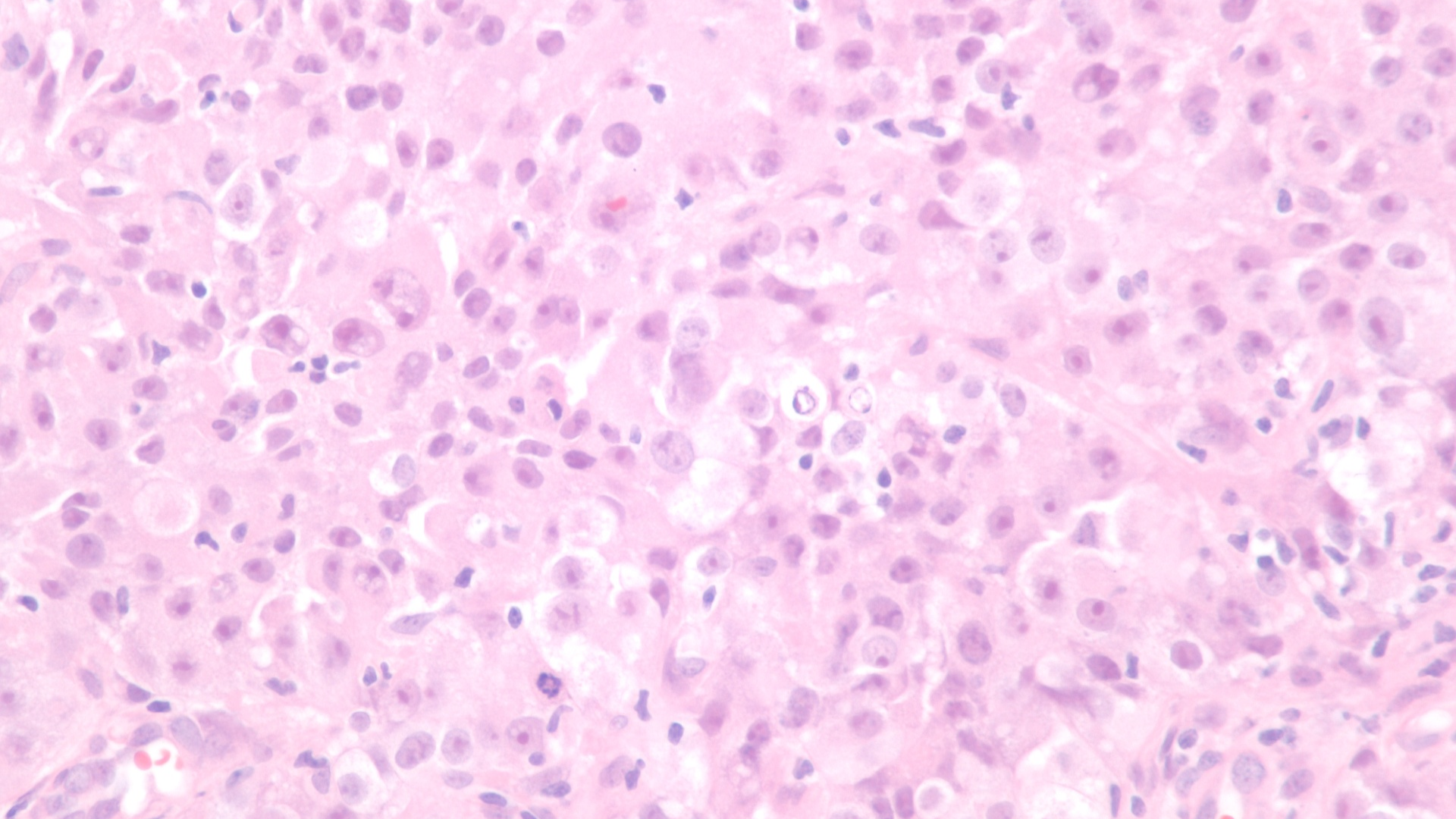
59 yo, PMB
endometrial biopsy performed









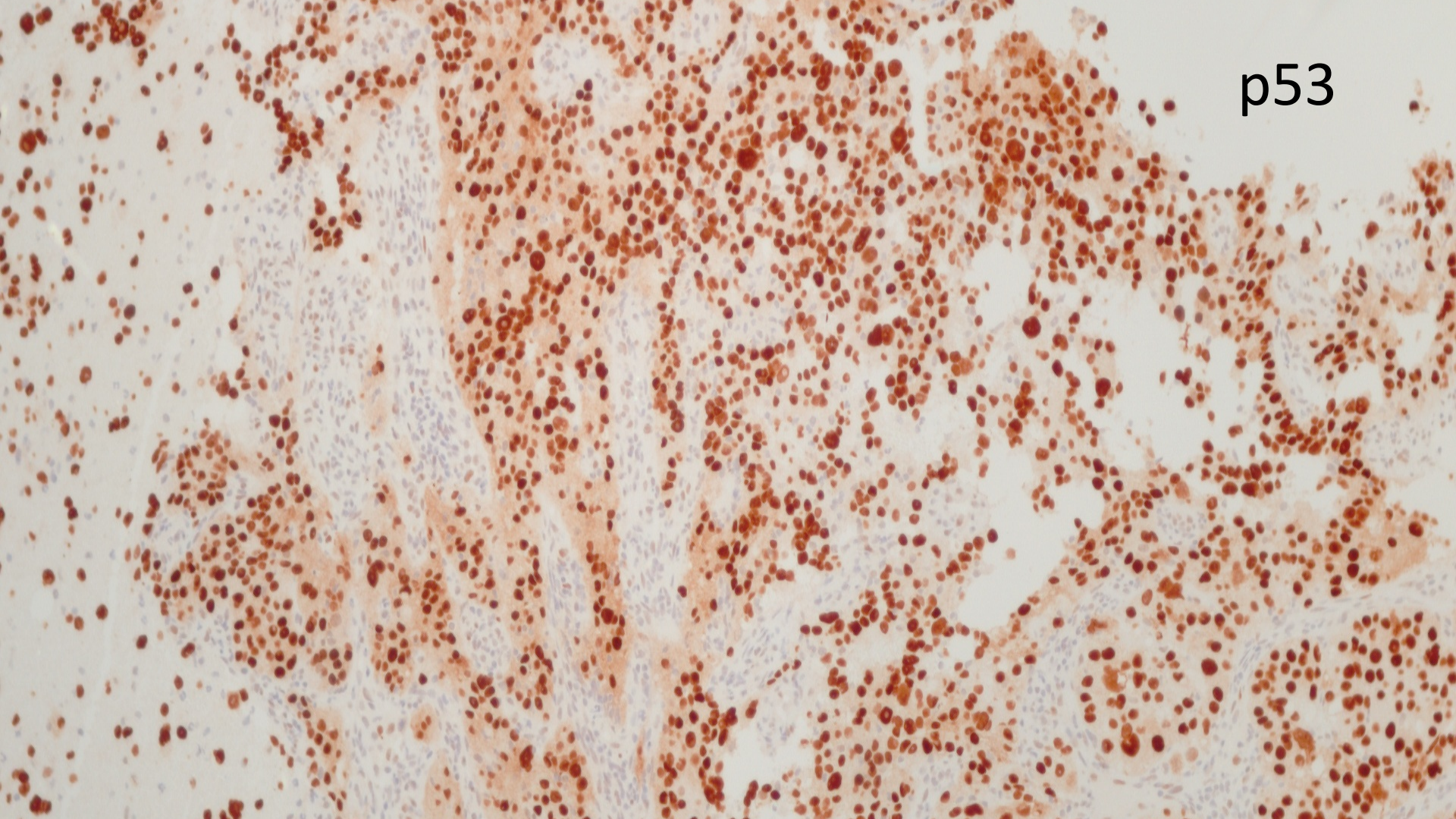


Diagnosis?

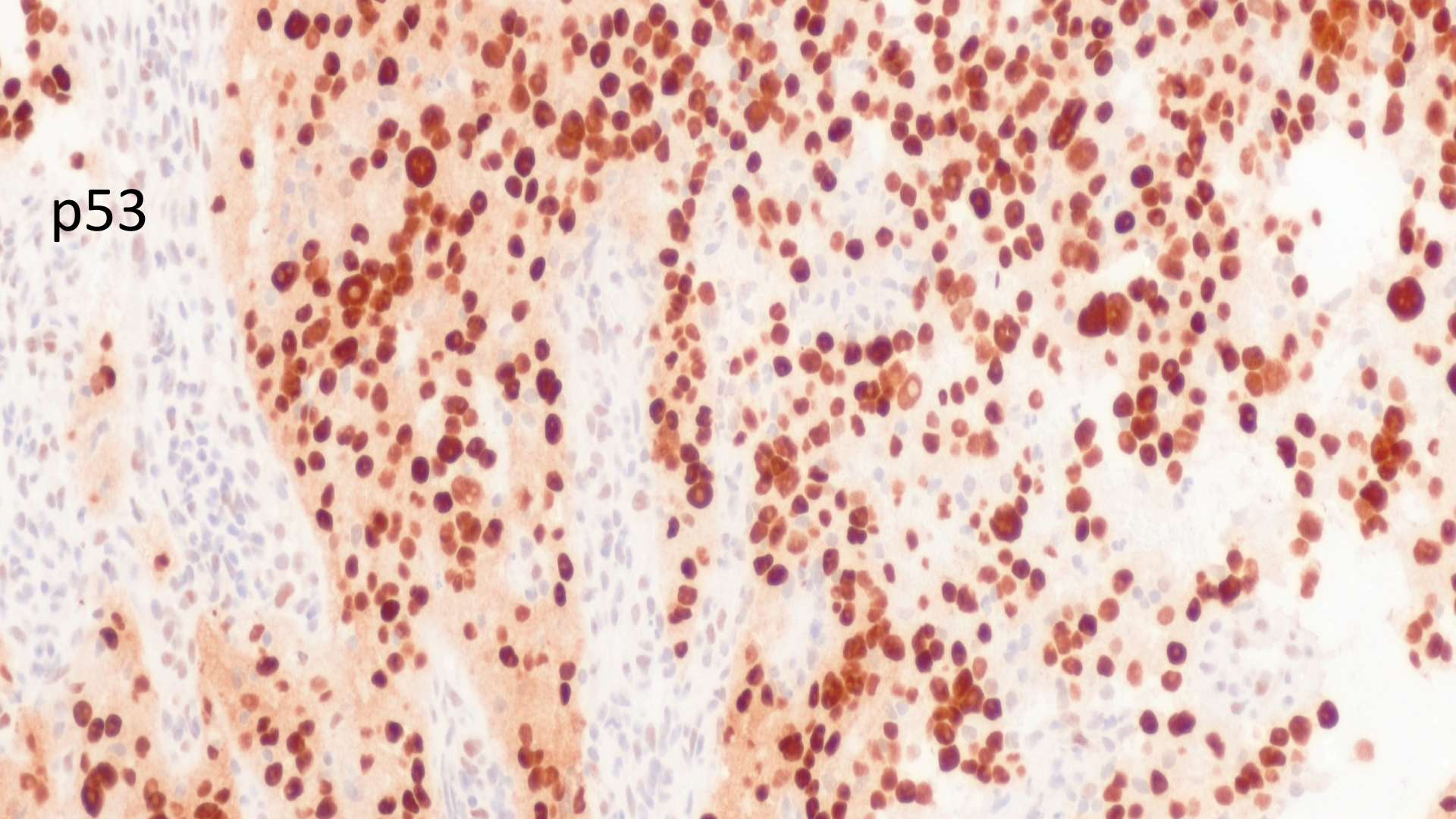
IHC

- p53abn (overexpressed)
- ER +

p53



p53

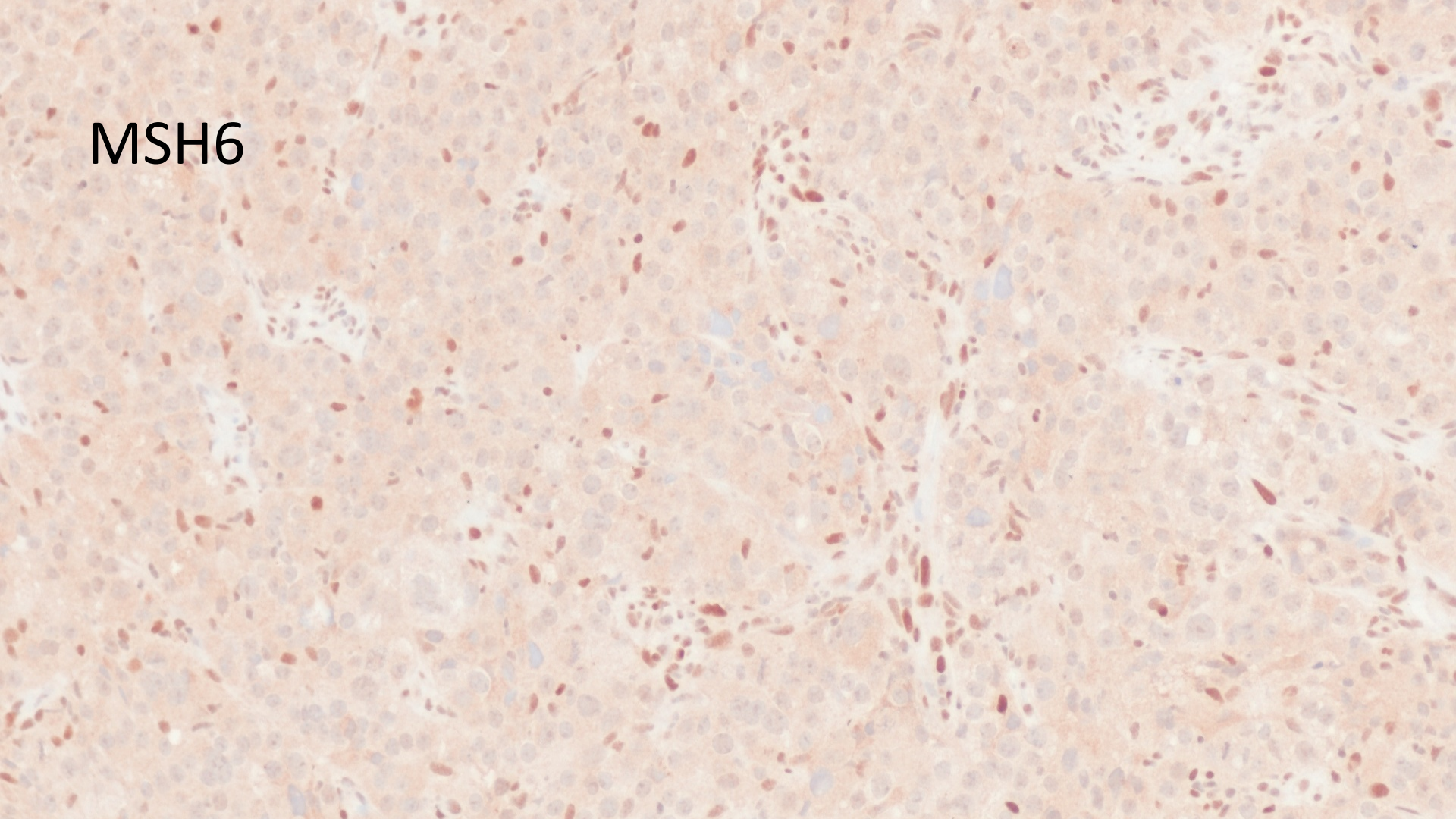


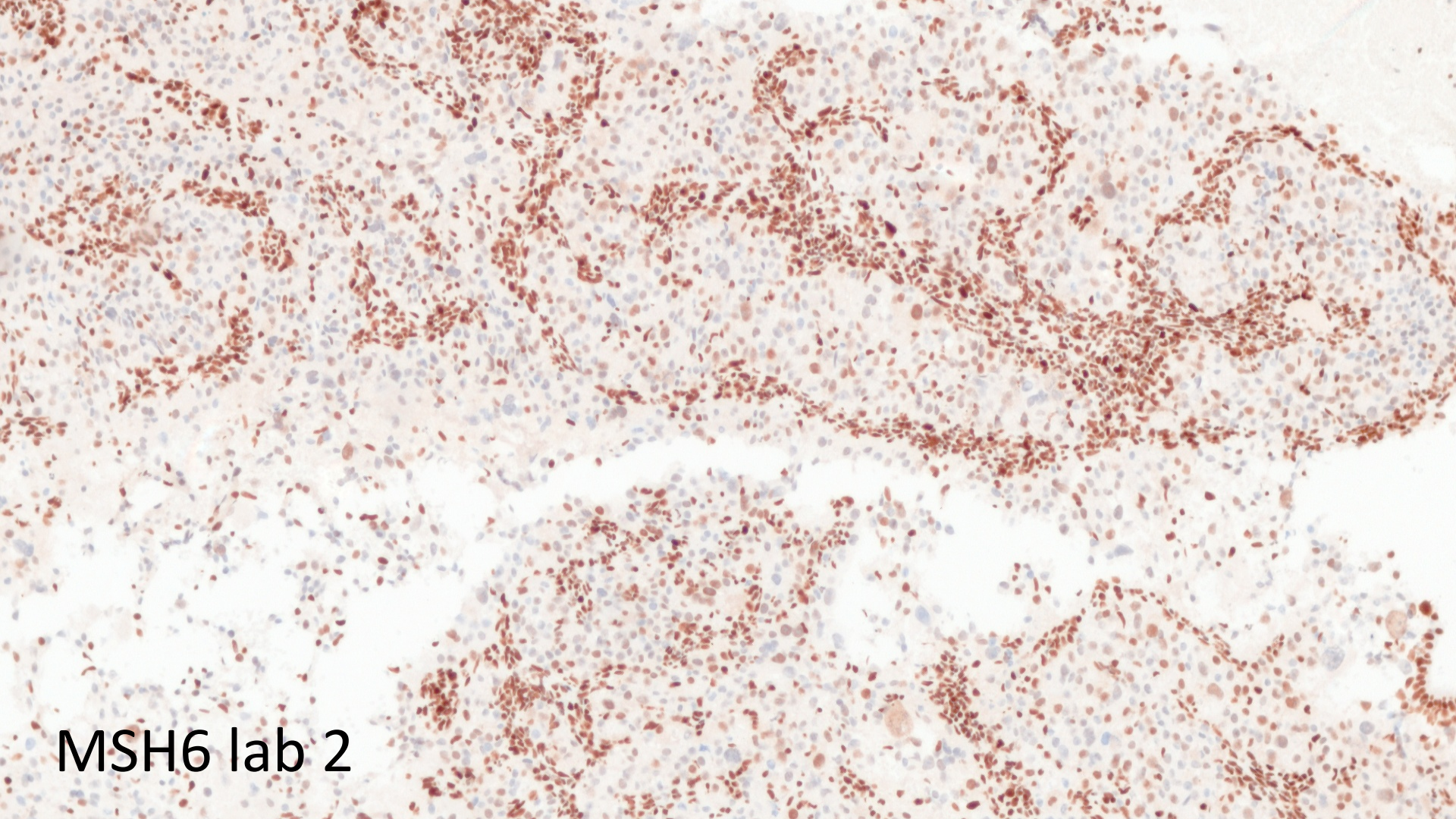
Diagnosis?

MSH6

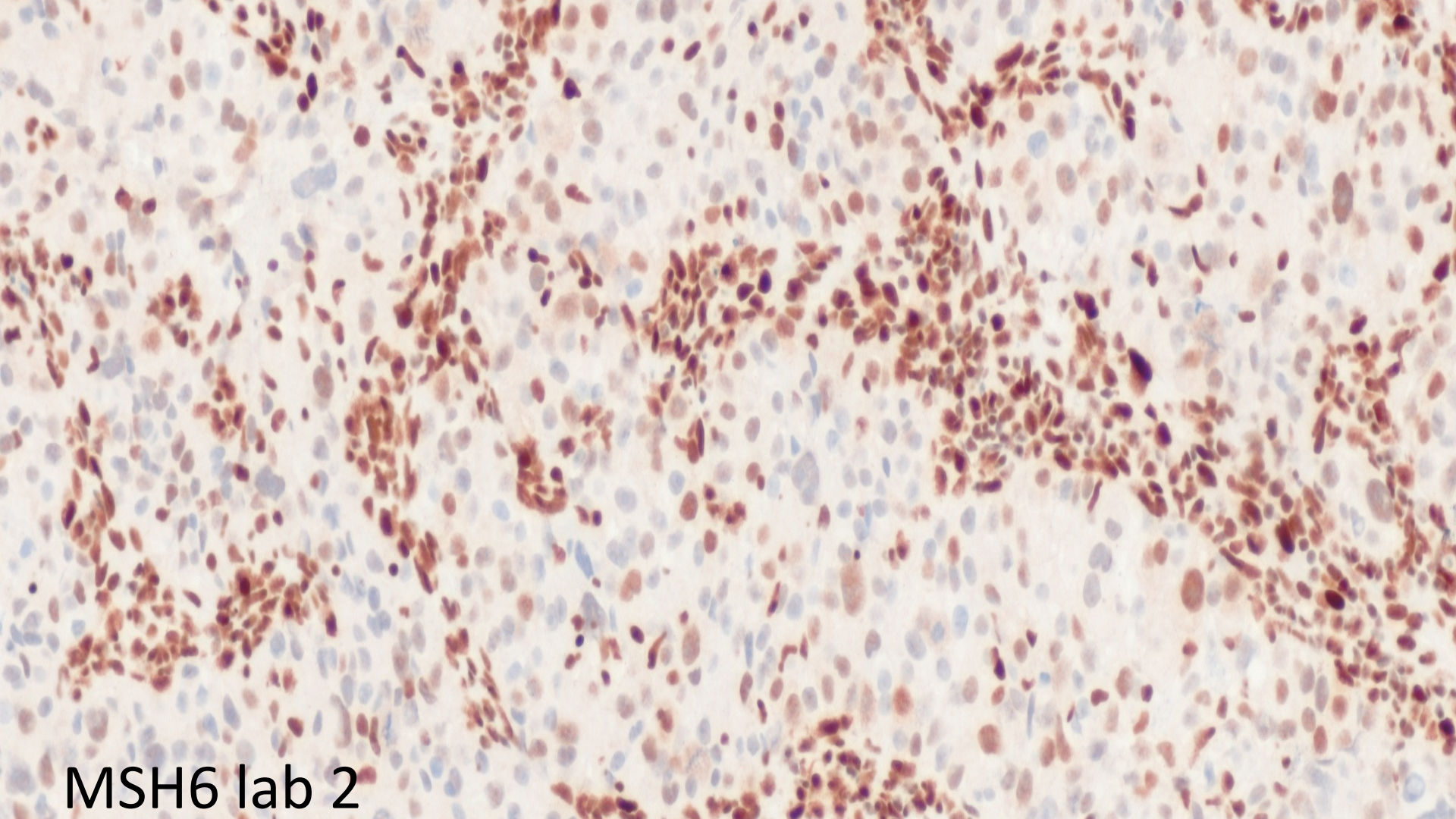


MSH6





MSH6 lab 2

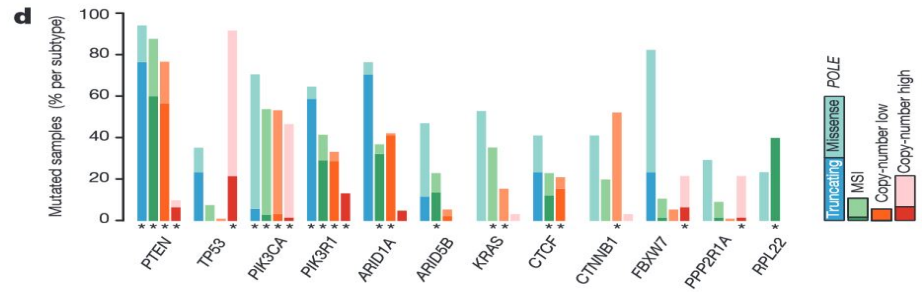
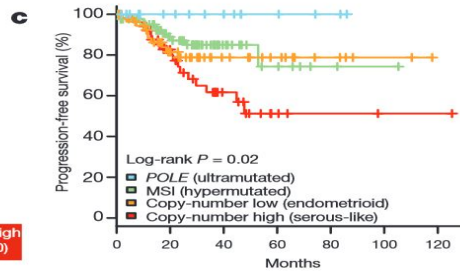
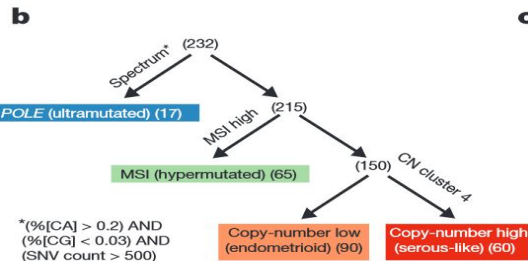
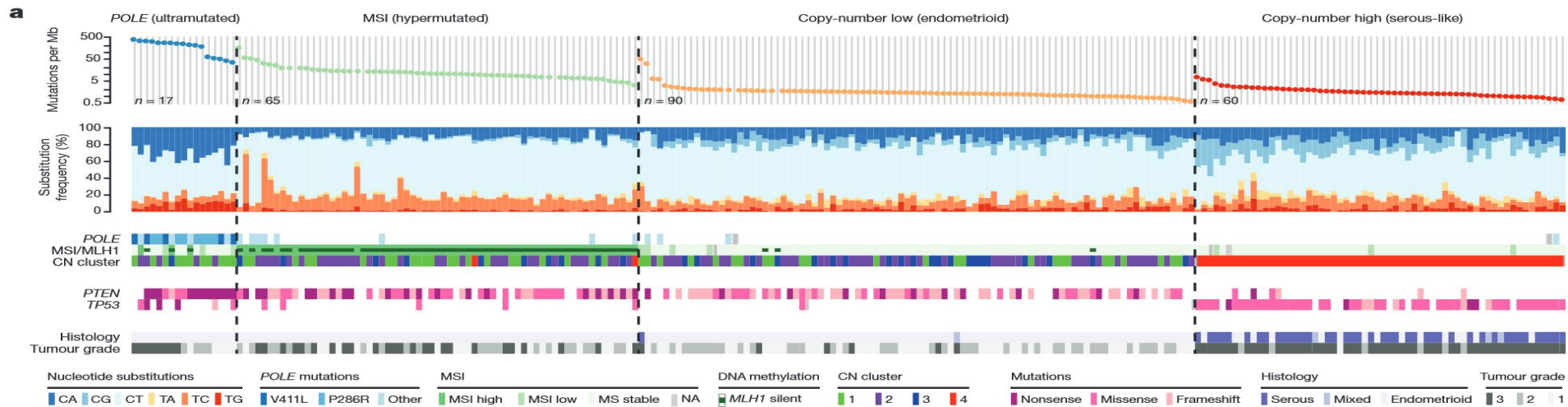


MSH6 lab 2

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

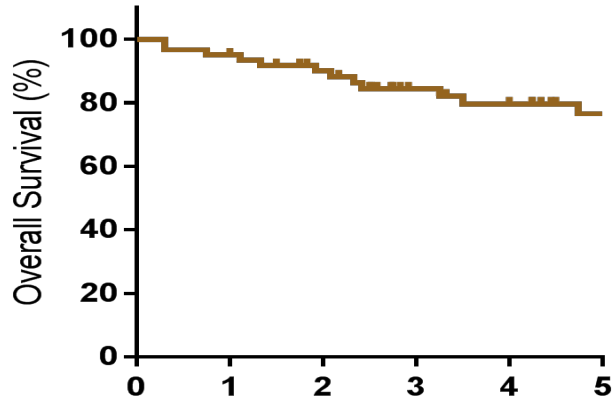


What to do when there is more than one molecular feature?? The clinical outcomes for patients with MMRd and p53abn is the same as for MMRd alone, and better than for patients with p53abn alone. Therefore, MMRd + p53abn is classified as MMRD!!!!

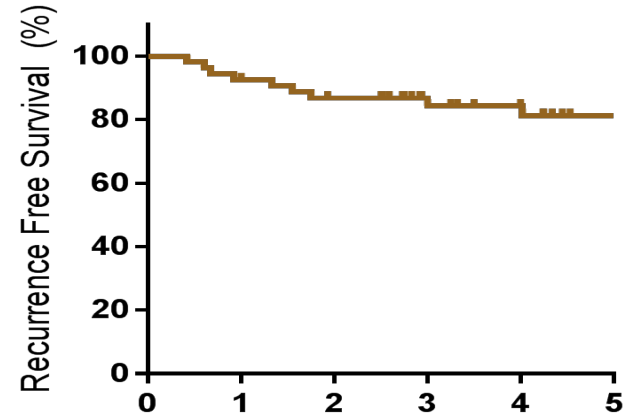
- Reference: **Clinicopathological and Molecular Characterisation of “Multiple Classifier” Endometrial Carcinomas**
- Alicia León-Castillo, Ester Gilvazquez, Remi Nout, Vincent T.H.B.M. Smit, Jessica N. McAlpine, Melissa McConechy, Stefan Kommoss, Sara Y. Brucker, Joseph W. Carlson, Elisabeth Epstein, 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
Overall survival



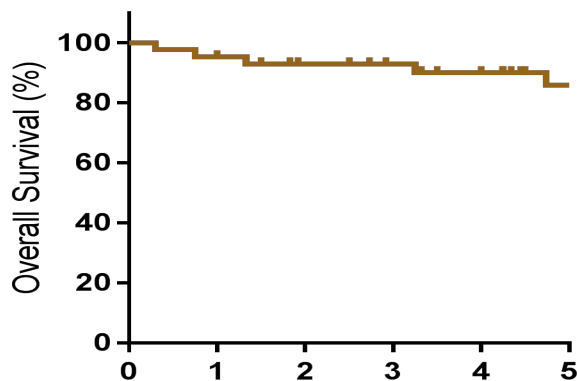
MMRd-p53abn
Recurrence Free Survival



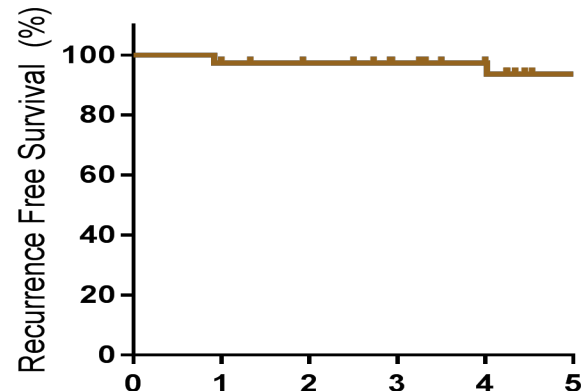
MMRd-p53abn EC have a 5-year RFS of 81% and OS of 77%

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