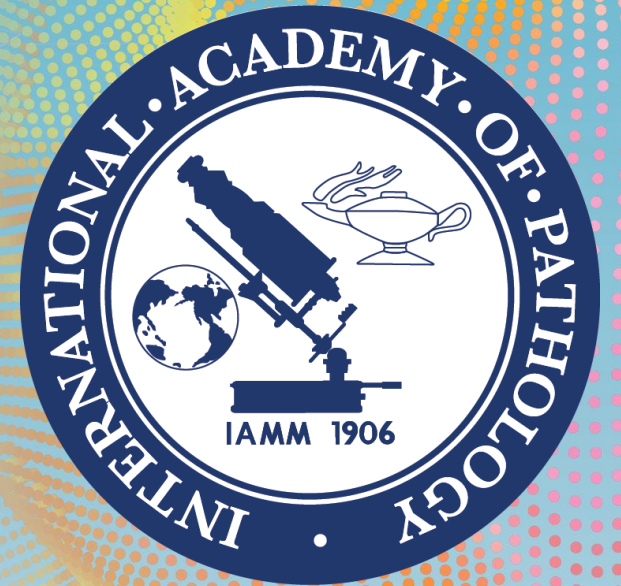


Endometrial cancer in women with BRCA mutations

Dr Eloise House
Mater Pathology



Disclosure of Relevant Financial Relationships

No relevant financial relationships

Case 1 – MS EW

52F – FHx MATERNAL SIDE OVARIAN CA, THYROID CA,
BREAST CA, CUP

P/W AUB

DIAGNOSED ON CURETTE WITH HG EC

1° CYTOREDUCTION

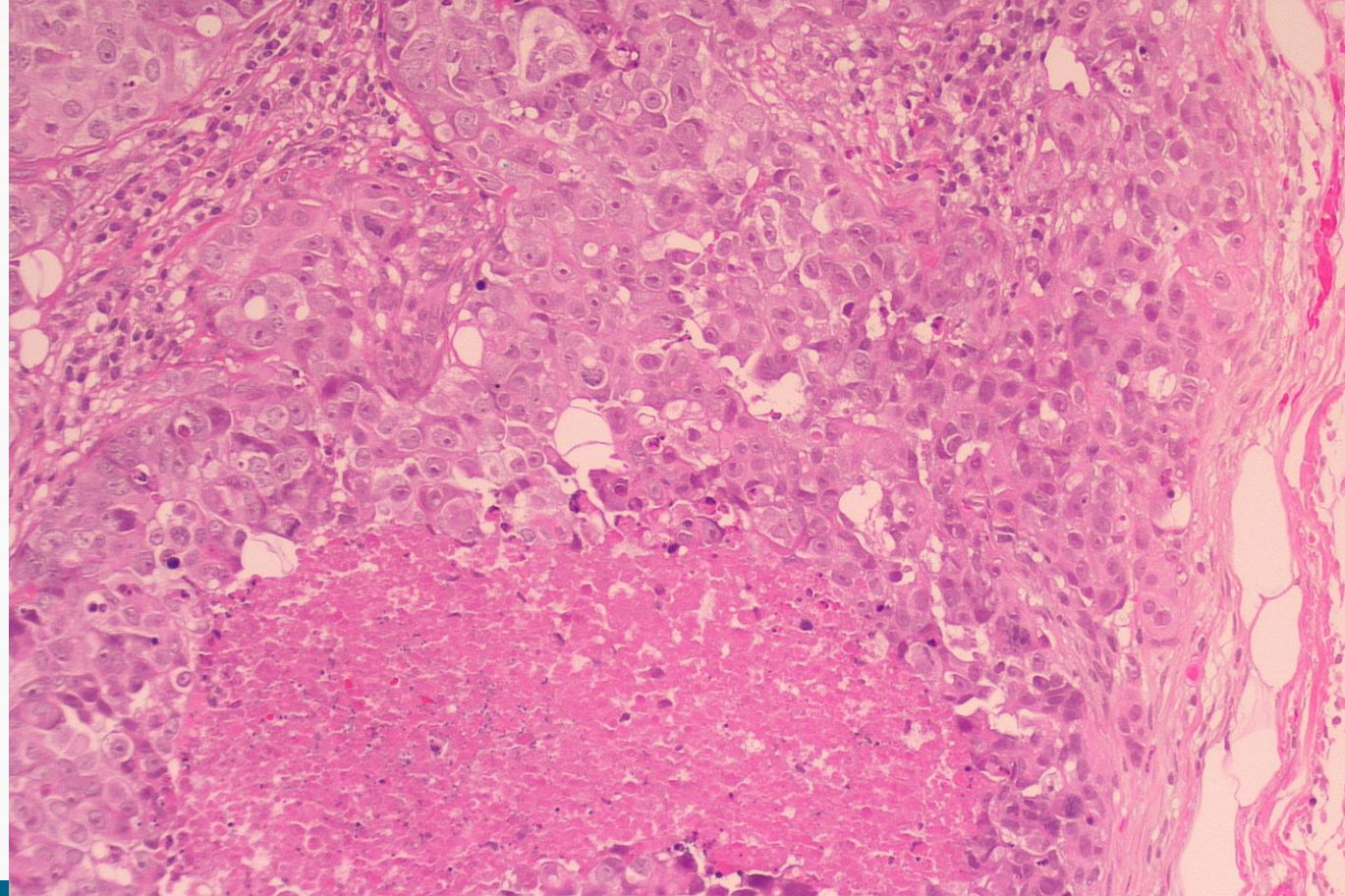
MRAD HYST, BSO, OMENTECTOMY, PELVIC LN, PELVIC
PERITONECTOMY, ASCITES

1/9mm, EXT LVI, MET BILAT OVARIES, PARAMETRIA, SEROSA,
OMENTUM, PERITONEUM, 5/9 LN, CYTO POS

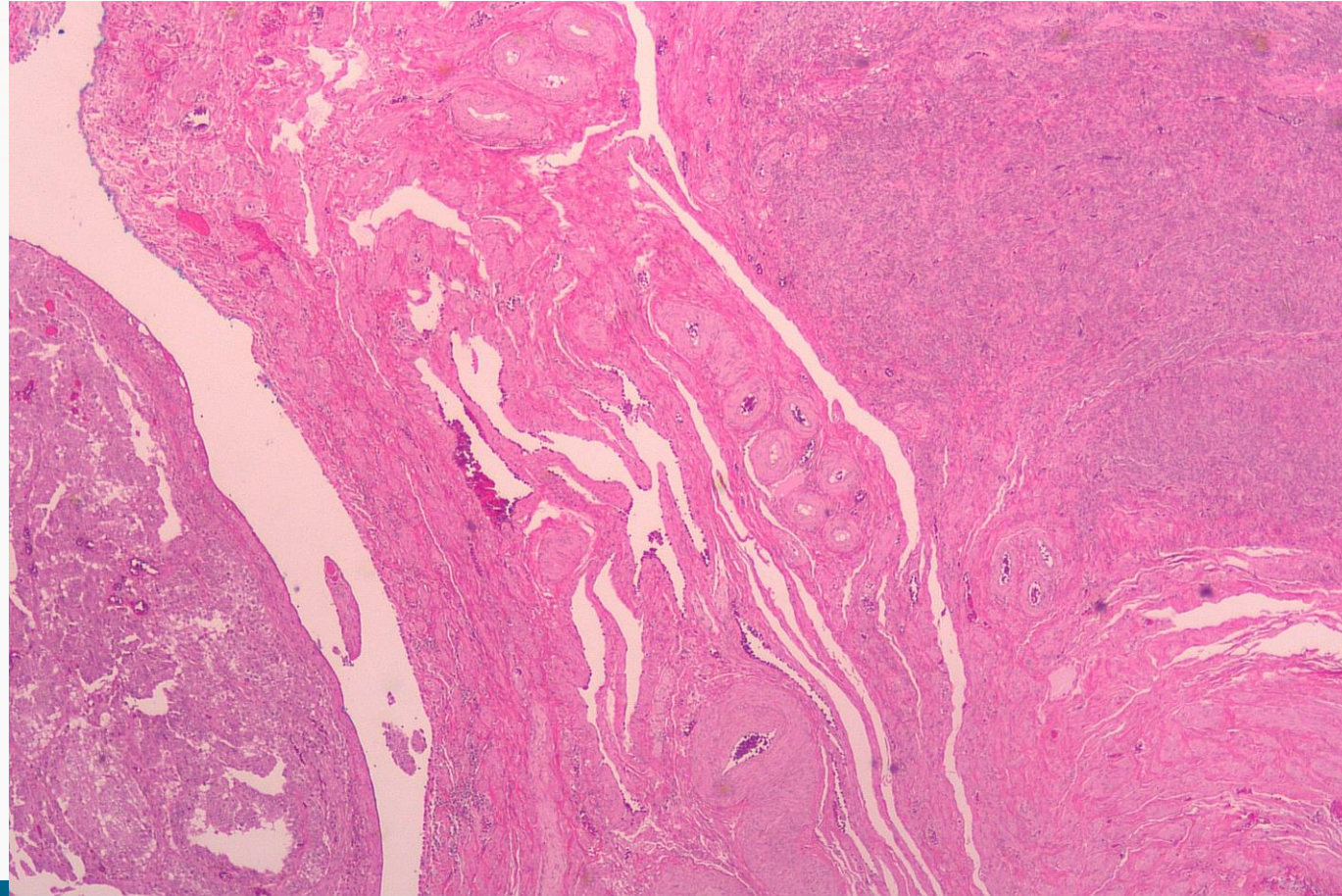
CASE 1 HISTOLOGY

HG ENDOMETRIAL CARCINOMA
MORPHOLOGICALLY AMBIGUOUS

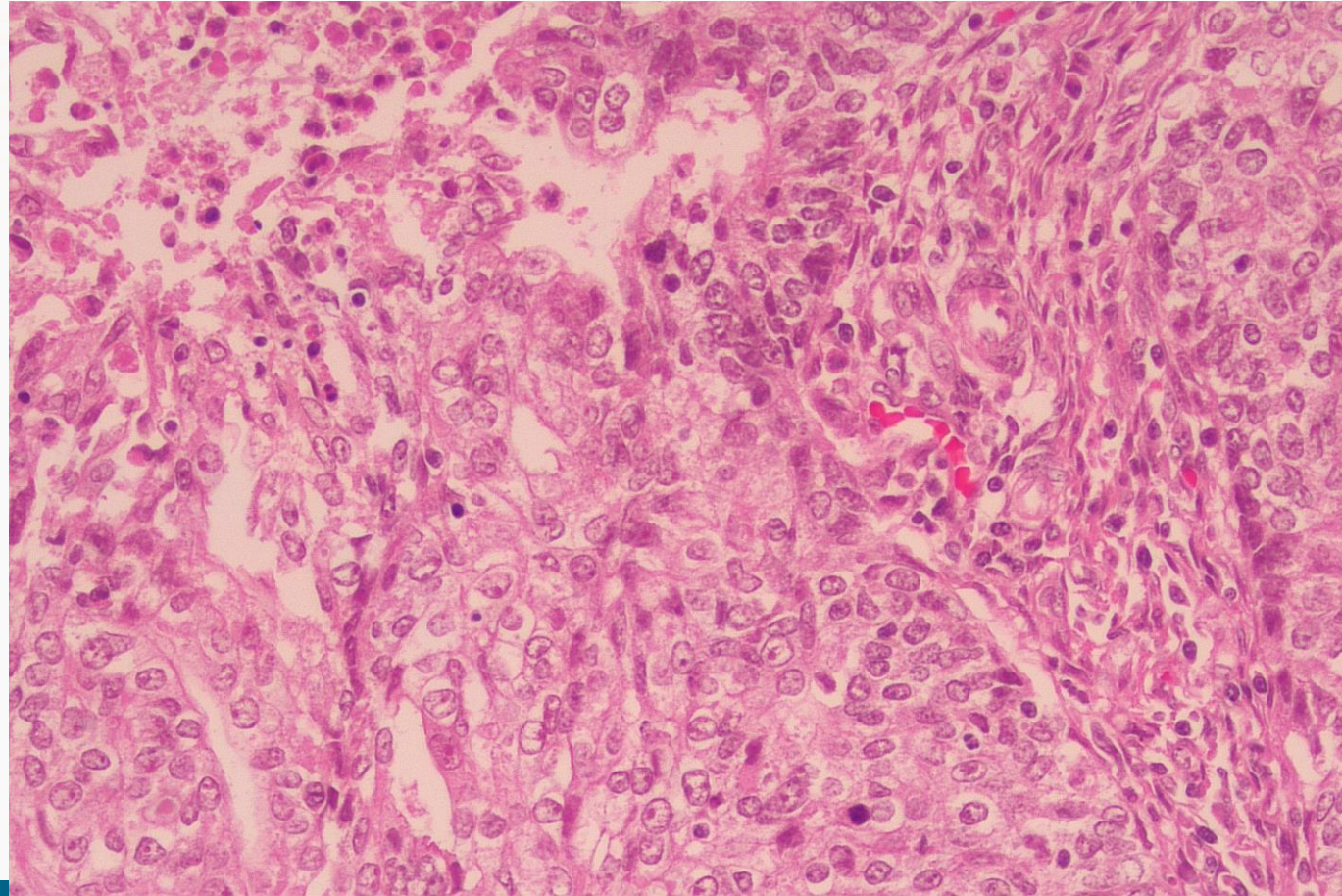
High grade, solid and glandular, with necrosis



Metastasis to hilum of ovary



High power of primary tumour



CASE 1 IHC

p53 MUTANT (NULL)

ER WEAK

β -CATENIN NORMAL

HER2 NEGATIVE

PTEN NORMAL

WT1 NEGATIVE

MMR PROFICIENT

CASE 2 – MS AM

44F – HX OF BILATERAL BREAST CA, PREV RR BSO

P/W POLYP IDENTIFIED ON PET SCAN

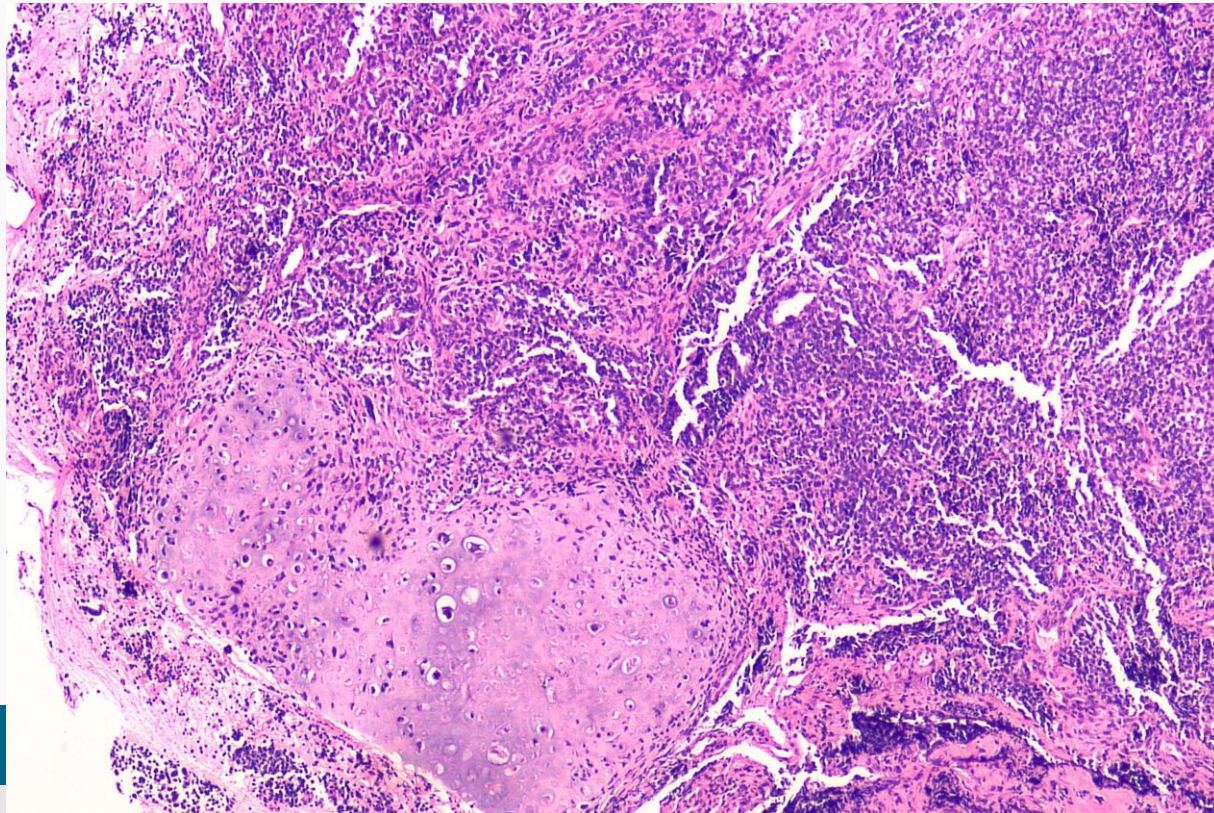
DIAGNOSED ON POLYPECTOMY WITH CARCINOSARCOMA
ARISING IN HIGH GRADE p53 ABN CARCINOMA

HYSTERECTOMY, BSLNB_x, PERITONEAL WASHINGS

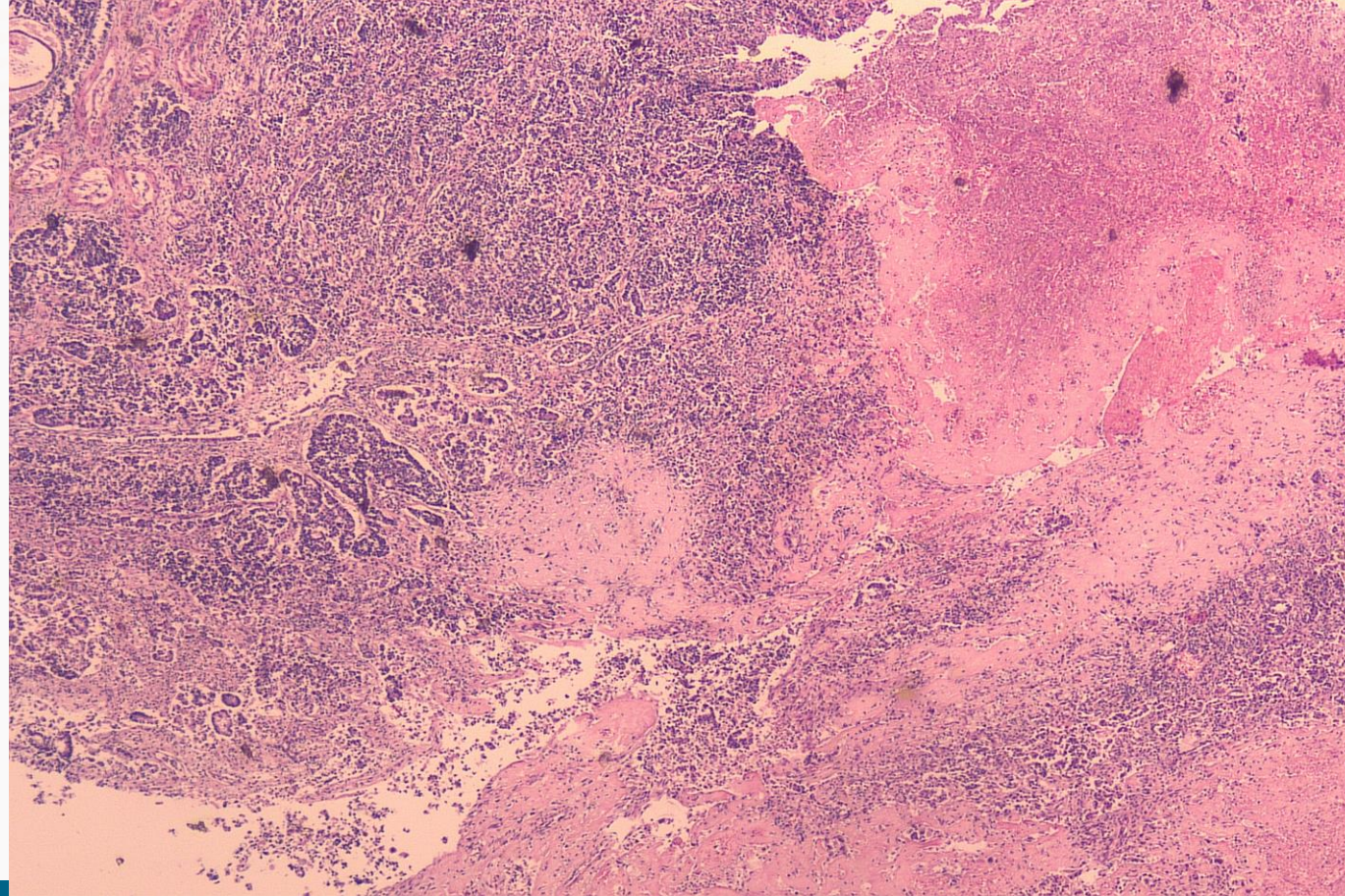
CASE 2 HISTOLOGY

CARCINOSARCOMA

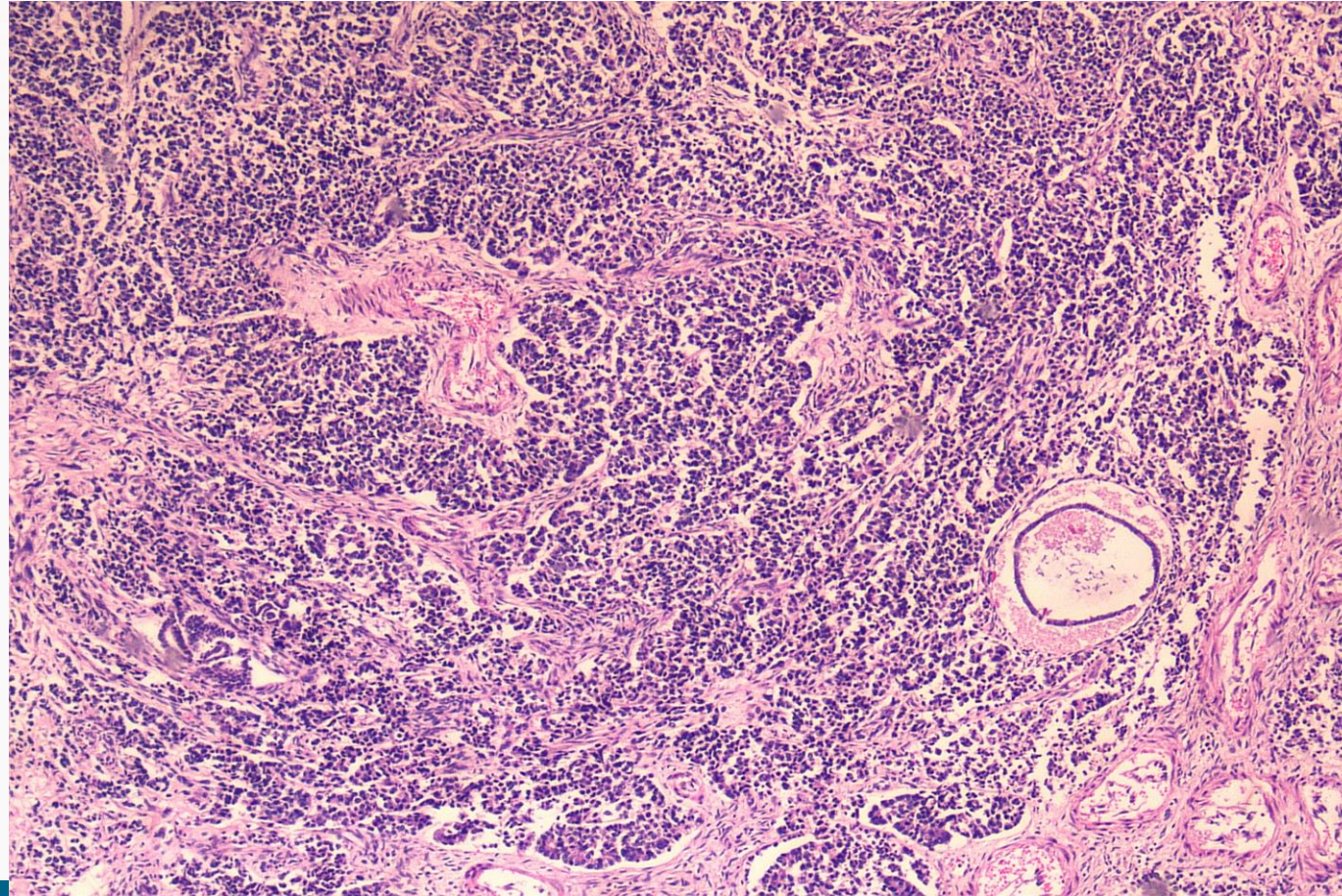
ARISING IN p53 MUTANT (NULL) CARCINOMA



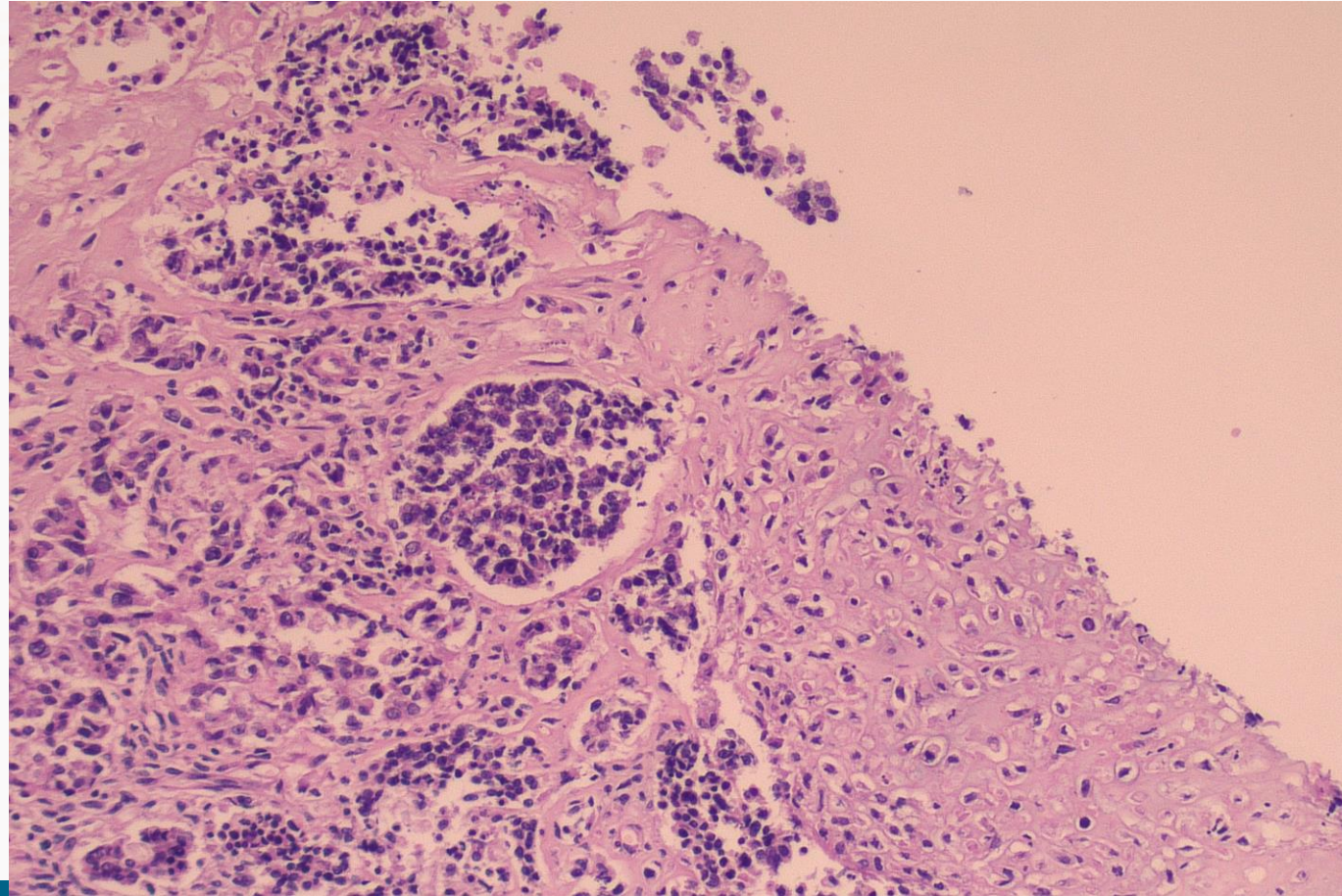
High grade solid and glandular with necrosis



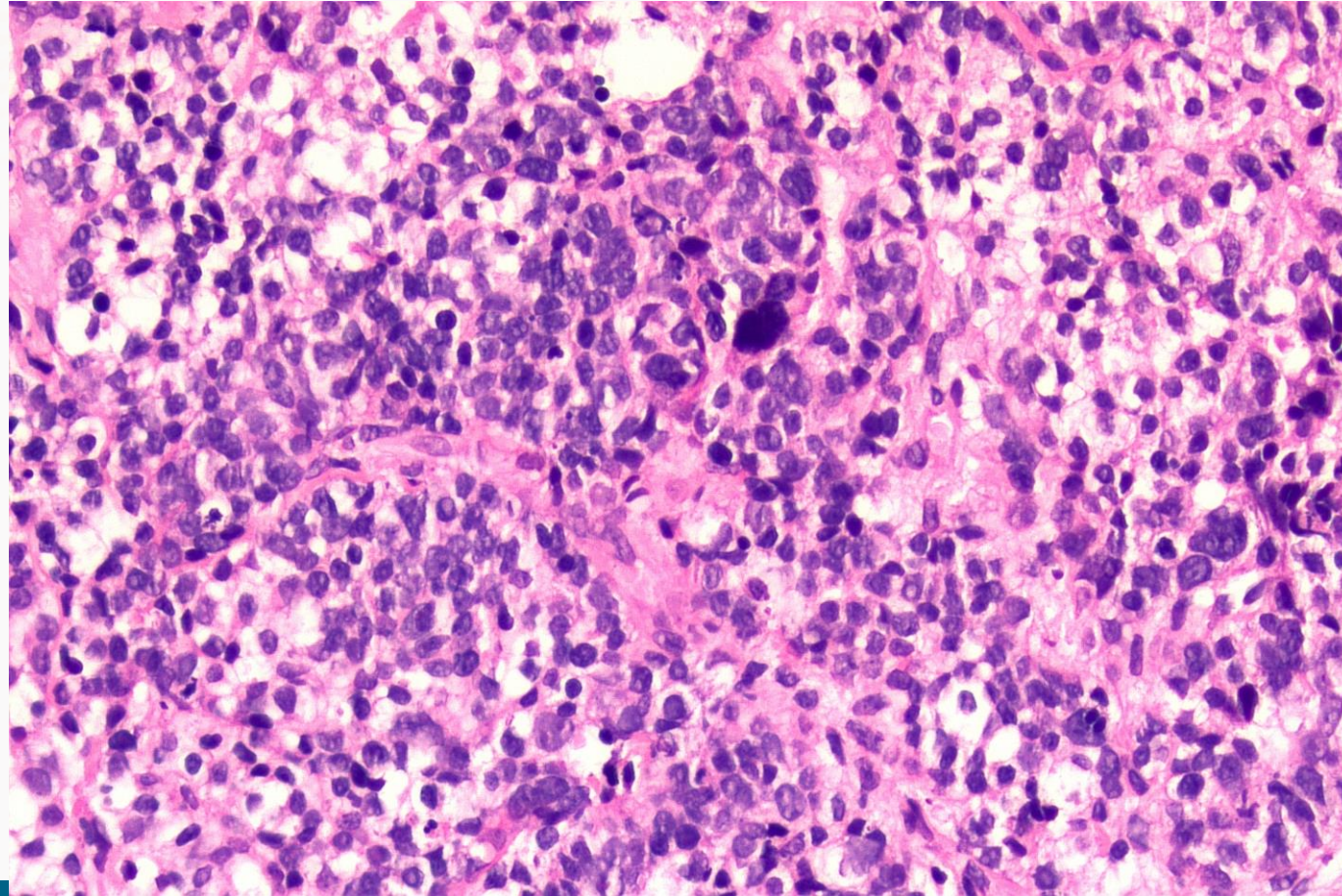
Poor gland formation



Carcinosarcoma



High power of original curette



CASE 2 IHC

p53 MUTANT (NULL)

ER NEGATIVE

MNF116 POSITIVE

CK7 PATCHY POSITIVE

PAX8 NEGATIVE

BRG1 AND INI1 RETAINED

MMR PROFICIENT

BRCA AND HRD TESTING

BOTH CASES WERE SUBMITTED FOR TARGETED SEQUENCING OF BRCA1 AND BRCA2, COMBINED WITH HRD MEASUREMENT

BOTH CASES REVEALED POSITIVE BRCA1 VARIANT STATUS

BOTH CASES WERE HRD POSITIVE

BOTH CASES HAD KNOWN BRCA1 GERMLINE MUTATIONS

EC AND GERMLINE BRCA MUTATIONS

Recent studies propose germline BRCA associated endometrial carcinoma is a distinct clinicopathological entity (de Jonge et al 2019)

The histological characteristics described in that study correlate with those seen in the case studies

Destructive invasion 74%

Desmoplasia 70%

Growth pattern SET features 52%

Comedo necrosis 44%

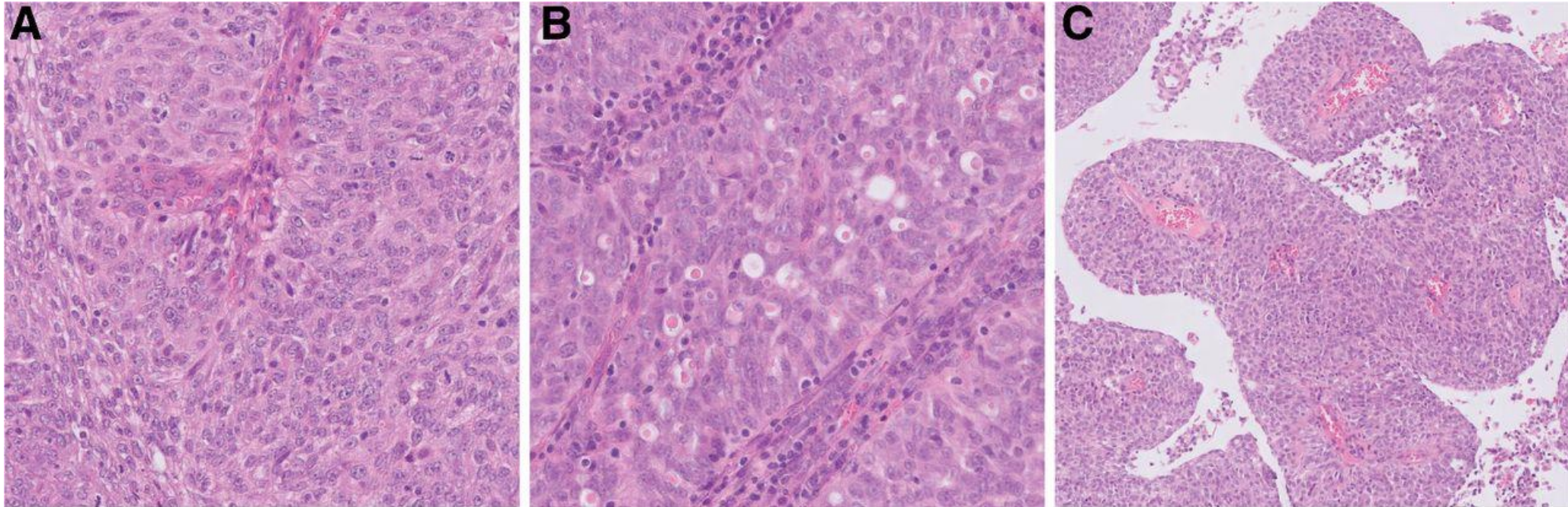
Grade 3 nuclei 83%

Tumour giant cells 48%

WT-1 IHC negative 70%

LVSI 42%

Clin Cancer Res. 2019;25(24):7517-7526. doi:10.1158/1078-0432.CCR-19-0848



Increased risk of EC with germline BRCA mutations?

Absolute risk remains low
2-3X increased risk

PARP inhibitor access

Role for HRD testing in gBRCA associated EC

BRCA testing of women with p53 mutated EC+/- hx breast CA

Clinical discussion re hysterectomy at time of RR BSO

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References

Marthe M. de Jonge, Lauren L. Ritterhouse, Cornelis D. de Kroon, Maaïke P.G. Vreeswijk, Jeremy P. Segal, Rutika Puranik, Harry Hollema, Matti A. Rookus, Christi J. van Asperen, Flora E. van Leeuwen, Vincent T.H.B.M. Smit, Brooke E. Howitt, Tjalling Bosse; for the HEBON Group, Germline BRCA-Associated Endometrial Carcinoma Is a Distinct Clinicopathologic Entity. *Clin Cancer Res* 15 December 2019; 25 (24): 7517–7526. <https://doi.org/10.1158/1078-0432.CCR-19-0848>

Kimia Sorouri et al., Endometrial Cancer Risk Among Germline BRCA1/2 Pathogenic Variant Carriers: Review of Our Current Understanding and Next Steps. *JCO Precis Oncol* 7, e2300290(2023). DOI:10.1200/PO.23.00290

de Jonge MM, de Kroon CD, Jenner DJ, Oosting J, de Hullu JA, Mourits MJE, Gómez Garcia EB, Ausems MGEM, Margriet Collée J, van Engelen K, van de Beek I; Hebon Group; Smit VTHBM, Rookus MA, de Bock GH, van Leeuwen FE, Bosse T, Dekkers OM, van Asperen CJ. Endometrial Cancer Risk in Women With Germline BRCA1 or BRCA2 Mutations: Multicenter Cohort Study. *J Natl Cancer Inst.* 2021 Sep 4;113(9):1203-1211. doi: 10.1093/jnci/djab036. PMID: 33710348; PMCID: PMC8418438.

Tian, W., Bi, R., Ren, Y., He, H., Shi, S., Shan, B., Yang, W., Wang, Q. and Wang, H. (2019), Screening for hereditary cancers in patients with endometrial cancer reveals a high frequency of germline mutations in cancer predisposition genes. *Int. J. Cancer*, 145: 1290-1298. <https://doi.org/10.1002/ijc.32389>