ANNUAL MEETING ON WOMEN'S CANCER

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EMPOWERING TEAMS
EMBRACING CHANGE

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Unlabeled/Investigational Uses

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I will not be discussing any unlabeled or investigational uses of any pharmaceutical products or medical devices.

If yes, describe the nature of what will be discussed.

Prevalence of germline pathogenic variants in patients with endometrial cancer diagnosed before and after 65 years old within a laboratory-based research registry

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From Selective to Universal: Genetic Testing in Endometrial Cancer(EC)

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The "Old" Way: Guidelines (PREMM5, molecular testing) often used **age <65** or family history as a gatekeeper for genetic testing.

The "New" Way: NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) recommends that universal germline testing should be **considered for all** EC patients regardless of age.

The Research Question: Does age-based screening overlook a significant number of high-risk patients?

Study Design: Large-Scale Registry Analysis

Data Source: Myriad Collaborative Research Registry (MCRR).

Patient Cohort: n = 28,356 patients with a primary diagnosis of endometrial cancer

Exclusion Criteria: Excluded patients with prior breast or ovarian cancer to ensure variants were specific to the EC diagnosis.

Genetic Tool: Multigene Panel Testing (MGPT) analyzing both Lynch syndrome (LS) and non-LS cancer predisposition genes.

The "Hidden" Risk in Older Patients

- 11% Overall Prevalence of Pathological/Likely Pathological (P/LP) Variants

	Age <65 (n=22,916)	**Age ≥65 (n=5,440)**
Total P/LP Variants	**12.6%** (2,905)	**6.5%** (354)
Lynch Syndrome	72.3% of variants	49% of variants
Other Hereditary Genes	28% of variants	**51%** of variants

	Age <65 Frequency (%)	**Age ≥65 Frequency (%)**
Other Common Hereditary Cancer Genes		
MUTYH	258 (30.8%)	70 (38.5%)
CHEK2	102 (12.2%)	21 (11.5%)
BRCA1	92 (12.2%)	18 (9.9%)
ATM	73 (8.7%)	13 (7.1%)
BRCA2	115 (11.0%)	13 (7.1%)
PTEN	22 (<1%)	1 (<1%)
TP53	13 (<1%)	8 (<1%)
Lynch Syndrome		
MSH6	723 (34.4%)	97 (55.7%)
MSH2	782 (37.2%)	24 (13.8%)
MLH1	382 (18.2%)	12 (6.9%)
PMS2	226 (10.8%)	41 (23.6%)
EPCAM	18 (0.9%)	0 (0%)

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Universal Testing: The New Standard of Care

- **Age-Independent Risk:** Age of diagnosis does not eliminate the possibility of a hereditary cancer predisposition.
- **Guideline Alignment:** This study supports NCCN Guidelines® for universal testing.
- **Family Impact:** Comprehensive testing is a vital tool for family risk assessment and the prevention of future cancers in relatives.