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NextGen geneCORE Somatic Endometrial Cancer Panel

Patient Selection	Technology	Specimen	Test Code	TAT
For newly diagnosed/ locally advanced / metastatic/ recurrent endometrial cancer cases	Next Generation Sequencing	FFPE Block	N8271	20 Days

- Allows concurrent analysis of DNA and RNA to detect genomic alterations such as SNVs, Indels, and Fusion drivers across 38 genes relevant for the clinical management of patients with endometrial cancer
- Enables classification of endometrial carcinoma into 4 clinically significant molecular subtypes: POLE mutations, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR), no specific molecular profile (NSMP), and p53 abnormal
- Helps to identify POLE mutated tumors that are associated with a more favorable prognosis
- Detects TP53 gene alteration which indicates an aggressive endometrial cancer
- Evaluates genes associated with Mismatch Repair Pathway
- Sensitivity: >99.99% and Specificity: >99.99%

Genomic Alterations	Gene List
SNVs and short indels	AKT1, ARID1A, BRAF, BRCA1, BRCA2, CCND1, CDH1, CDKN2A, CHEK2, CTNNB1, ERBB2, ESR1, FBXW7, FGFR1, FGFR2, FGFR3, KRAS, L1CAM, MLH1, MLH3, MSH2, MSH3, MSH6, MUTYH, MYC, NRAS, NTRK1, NTRK2, NTRK3, PIK3CA, PIK3R1, PMS1, PMS2, POLD1, POLE, PTEN, RET and TP53
Gene fusions	NTRK1, NTRK3, FGFR1, FGFR2, FGFR3 and RET
Mismatch repair genes	MSH2, MSH3, MSH6, MLH1, PMS1, MLH3 and PMS2

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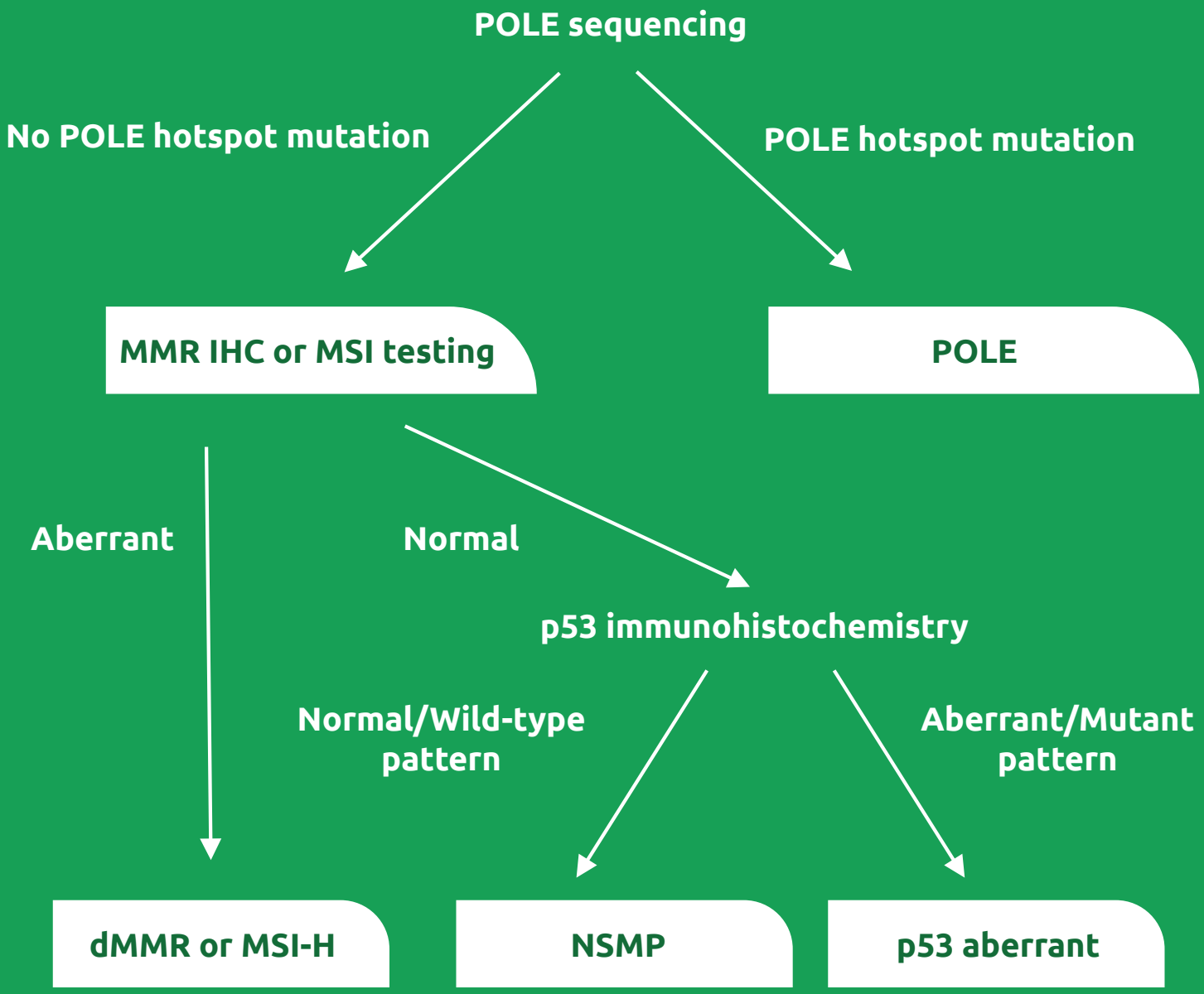
Pathology and Genomics in Endometrial Carcinoma

The NCCN Guidelines for uterine neoplasms include a diagnostic algorithm for integrated genomic-pathologic classification of endometrial carcinomas based on the TCGA study.



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POLE NGS Testing guidance[1]
All endometrial carcinomas regardless of histological type[2]

BIOPSY:
- MMR[3]
- p53[4]
- ER[5]

IHC on all cases

SURGICAL STAGING:[9]
- Final histological type
- Final grade (endometrioid)
- Final clinico-pathological stage
- Presence or absence of substantial LVSI[10]

GROUP 1:
- MMR abnormal[6]

and/or
- p53 abnormal[7]

→ ***POLE*** **NGS testing RECOMMENDED[8]**

GROUP 2:[11]
- Stage IA, low-grade (G1/G2), ER-positive endometrioid, with no or focal LVSI

→ ***POLE*** **NGS testing NOT RECOMMENDED**

GROUP 3:[12]
- Stage IA G3 endometrioid with no/focal LVSI
- Stage IA any grade endometrioid with substantial LVSI
- Stage IB/II any grade endometrioid
- All Stage I/II ER- negative endometrioid
- All Stage I/II non- endometrioid

→ ***POLE*** **NGS testing RECOMMENDED**

GROUP 4:[13]
- Stage III/IV or locally advanced EC

→ ***POLE*** **NGS testing *only if recommended by MDT***

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NextGen geneCORE Somatic Endometrial Cancer Panel

Case Number:
Patient Name:
Age/Sex:
Patient Location:
Hospital Name:
Physician Name:
Date & Time of Accessioning:
Date & Time of Reporting:

Your Test Results

Test Information

NextGen geneCORE Somatic Endometrial Cancer Panel is a Next Generation Sequencing (NGS) assay that enables the detection of clinically relevant genomic alterations (SNVs, indels and gene fusions) from both DNA & RNA, within the 38 unique genes for optimum therapy selection, prognostication and additionally aids in drug discovery re-search and clinical trial research programs.

Specimen Information

Received FFPE block

Clinical History

Patient with grade 2 endometrial adenocarcinomaTM

Molecular Classification Results

Genomic Findings	Molecular Classification
No clinically significant mutation detected in TP53 & POLE genes and No deficiency has been detected in MMR	No specific molecular profile (NSMP)

Results

Clinically Relevant Genomic Findings (Variants Summary)

Gene (Exon) [Transcript]	Variant (Amino acid Alteration)	Variant (Coding)	Variant Allele Frequency (VAF)	Variant Effect*	Variant Classification (AMP)	Variant Classification (ACMG)#	Associated FDA Approved Therapies
BRCA1 (10) [NM_007294.4]	p.Arg1347Ter [p.R1347*]	c.4039A>T	78.7%	LOF	Tier2	Pathogenic	Available (Please refer to page no. 3 for more details)

Mismatch Repair (Mmr) Pathway Results

Assay Biomarker	Result	Interpretation
MMR Pathway Genes Status (MSH2, MSH3, MSH6, MLH1, PMS1, MLH3, PMS2)	Negative	No clinically significant variant detected in MMR pathway genes.