FAST FACTS: REFINING ENDOMETRIAL CARCINOMA SUBCLASSIFICATION WITH NGS

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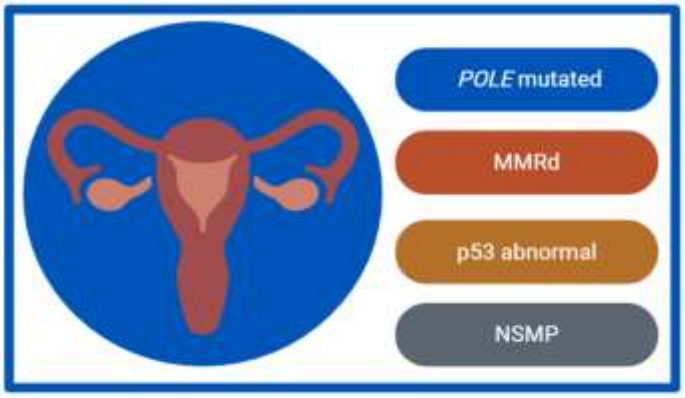
Endometrial carcinoma (EC) is the 5th most common cancer affecting women in South Africa. The subclassification of EC has undergone significant refinement, particularly with the integration of molecular diagnostics into routine clinical practice. The most significant change is the recognition of four non-overlapping molecular categories.



This molecular categorisation allows for a much more accurate prediction of clinical outcomes and tailored therapeutic strategies. Both the European Society for Medical Oncology (ESMO) and the European Society of Gynaecological Oncology (ESGO) now recommend molecular classification as standard practice in the management of EC.

1. *POLE* mutated EC

those harbouring mutations in the gene encoding the (exonuclease domain of the) enzyme DNA Polymerase *epsilon* (*POLE*mut EC), also known as **ultramutated** owing to the exceptionally high rates of mutations within tumour cells

2.MMRd EC

those that are mismatch repair deficient (MMRd EC), also known as **hypermutated**, as these too show high rates of mutations in tumour cellls

3. p53 abnormal

those showing mutations in the oncogene *TP53* (p53abn EC), also known as **copy number-high** owing to the high numbers of somatic copy number alterations; and

4. No specific molecular profile (NSMP) EC

those having none of the 3 molecular defects. This is a **diagnosis of exclusion**.

NEXT GENERATION SEQUENCING (NGS) BASED PROFILING OF ENDOMETRIAL CARCINOMA

- Ampath is now offering an Endometrial Carcinoma-specific NGS panel for the molecular subclassification of ECs consisting of the *POLE, TP53* and *CTNNB1* genes.
- While mutated *CTNNB1* does not currently define a distinct molecular sub-category, it has been shown to predict a significantly increased rate of disease recurrence and lower overall survival.

ENDOMETRIAL CARCINOMA NGS PANEL

Test mnemonic	ECNGS
Clinical indication	All endometrial carcinomas (regardless of histological subtype)
Genes tested	*POLE, TP53* and *CTNNB1* *MMRd is tested for using immunohistochemical staining
Specimen type	Formalin Fixed Paraffin Embedded Tissue (FFPE) 6-8 normal slides (not charged) with 10 micron thick unstained recuts
Turnaround time	7-10 working days

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