**WHAT IS A BIOMARKER?**

Biomarkers are proteins, genes, immune markers, or hormones that can be specific to a particular cancer and may differ between patients.¹²³

**WHAT IS MISMATCH REPAIR DEFICIENCY?**

**dMMR⁴,⁵**

Normal cells have a mismatch repair pathway (MMR) that ensures DNA is copied without errors during natural cell growth and replication.

In some cancer patients, MMR is defective, or deficient (dMMR), meaning that malignant cells in these patients may contain DNA copying errors that cannot be corrected.

**MICROSATELLITES¹⁴,⁵**

Microsatellites are short repetitive sequences of DNA that are particularly sensitive to DNA copying errors during natural cell growth and replication.

- Microsatellite instability (MSI) is a change that occurs in certain cells, such as cancer cells, in which the number of repeated DNA bases in a microsatellite is different from what it was when the microsatellite was inherited (bottom figure).⁷
- The presence of MSI represents phenotypic evidence that MMR is not functioning normally.⁷

**What causes dMMR?⁶**

dMMR can be caused by sporadic mutations or an underlying genetic condition (eg, Lynch syndrome).

**ALL PATIENTS WITH ENDOMETRIAL CANCER SHOULD BE TESTED FOR dMMR⁸**

Guidelines published by groups such as the Society of Gynecologic Oncology (SGO) recommend universal testing for dMMR in patients with endometrial cancer.

**ABOUT 1/3 OF ENDOMETRIAL CANCERS WILL BE POSITIVE FOR dMMR⁹,¹⁰**

Endometrial Cancer Types

- Mismatch repair proficient (MMRp) 70%
- dMMR 30%
LABORATORY TESTS FOR dMMR

Immunohistochemistry (IHC) is a commonly used method to visualize loss of expression of proteins involved in MMR from a tissue sample taken from a patient.\textsuperscript{5,11,12}

- MMR IHC is a proven assay to identify dMMR tumors and has shown concordance with other testing platforms for MSI-H.\textsuperscript{7}
- dMMR and MSI-H populations are biologically similar and have been shown to have >95% concordance when assessed by their respective assays.\textsuperscript{3,13}
- Molecular testing to assess MSI is indicated in case IHC tests are inconclusive\textsuperscript{7}

IHC detects the presence or absence of MMR proteins.\textsuperscript{5,11}
- An abnormal IHC test shows at least one of the proteins “not detected” (image on left; absence [or loss] of staining)
- Normal healthy tissues exhibit normal staining (image on right; MMR proteins “intact” and “detected”)

dMMR IS A BIOMARKER THAT CAN INFORM TREATMENT DECISIONS IN ENDOMETRIAL CANCER\textsuperscript{14}

Treatment options for advanced or recurrent dMMR endometrial cancer include immune checkpoint inhibitors (ICIs) such as PD-1/PD-L1 inhibitors.\textsuperscript{14}
- ICIs are a treatment option that may be appropriate for select patients with recurrent or advanced endometrial cancer based on their dMMR status.\textsuperscript{14}

DIAGNOSTIC TESTING FOR MMR CAN IDENTIFY PATIENTS WITH ENDOMETRIAL CANCER WHO MAY RESPOND TO TREATMENT WITH ICIs.\textsuperscript{7,14,15}