# Mismatch Repair and Microsatellite Instability Testing for Immune Checkpoint Inhibitor Therapy

## Statements and Strengths of Recommendations

### SUMMARY OF RECOMMENDATIONS

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<th>Guideline Statement</th>
<th>Strength of Recommendation</th>
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| 1. For patients with CRC being considered for immune checkpoint inhibitor therapy, pathologists should use MMR-IHC and/or MSI by PCR for the detection of DNA MMR defects. Although MMR-IHC or MSI by PCR are preferred, pathologists may use a validated MSI by NGS assay for the detection of DNA MMR defects.  

*Note:* MSI by NGS assay must be validated against MMR-IHC or MSI by PCR and must show equivalency.                                                                                                                | Strong Recommendation       |
| 2. For patients with gastroesophageal and small bowel cancer being considered for immune checkpoint inhibitor therapy, pathologists should use MMR-IHC and/or MSI by PCR over MSI by NGS for the detection of DNA MMR defects.  

*Note:* This recommendation does not include esophageal squamous cell carcinoma.                                                                                                                                   | Strong Recommendation       |
| 3. For patients with endometrial cancer being considered for immune checkpoint inhibitor therapy, pathologists should use MMR-IHC over MSI by PCR or NGS for the detection of DNA MMR defects.                                                                 | Strong Recommendation       |
| 4. For patients with cancer types other than CRC, GEA, small bowel, and endometrial being considered for immune checkpoint inhibitor therapy, pathologists should test for DNA MMR, although the optimal approach for the detection of MMR defects has not been established.  

*Note:* Assays must be adequately validated for the specific cancer type being tested with careful consideration of performance characteristics of MMR-IHC and MSI by NGS or PCR for the detection of DNA MMR defects. | Conditional Recommendation  |
| 5. For all cancer patients being considered for immune checkpoint inhibitor therapy based upon defective MMR, pathologists should **NOT** use TMB as a surrogate for the detection of DNA MMR defects. If a tumor is identified as TMB-high, pathologists may perform IHC and/or MSI by PCR to determine if high TMB is secondary to MMR deficiency. | Strong Recommendation       |
| 6. For cancer patients being considered for immune checkpoint inhibitor therapy, if an MMR deficiency consistent with Lynch Syndrome is identified in the tumor, pathologists should communicate this finding with the treating physician. | Strong Recommendation       |

**Abbreviations:** CRC, colorectal cancer; DNA, deoxyribonucleic acid; GEA, gastroesophageal adenocarcinoma; IHC, immunohistochemistry; MMR, mismatch repair; MSI, microsatellite instability; NGS, next generation sequencing; PCR, polymerase chain reaction; TMB, tumor mutation burden


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