

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Updated Testing Recommendations for Select Gastrointestinal (GI) Cancers

PD-L1 Testing is Now Recommended for All Newly Diagnosed (Any Stage) Gastric and Esophageal/GEJ Cancers

This resource provides general information regarding National Comprehensive Cancer Network® (NCCN®) biomarker testing at various stages of disease. For product-specific testing recommendations, please consult the product's Prescribing Information and NCCN Guidelines®.

Gastric Cancer¹

Biomarker	Disease stage	Testing methods
PD-L1	Newly diagnosed (any stage)	IHC
HER2 ^a	Metastatic adenocarcinoma ^{c,d}	IHC, ISH, FISH, NGS
CLDN18.2	Metastatic ^c	IHC
MSI ^b	Newly diagnosed (any stage)	PCR, NGS
MMR ^b	Newly diagnosed (any stage)	IHC

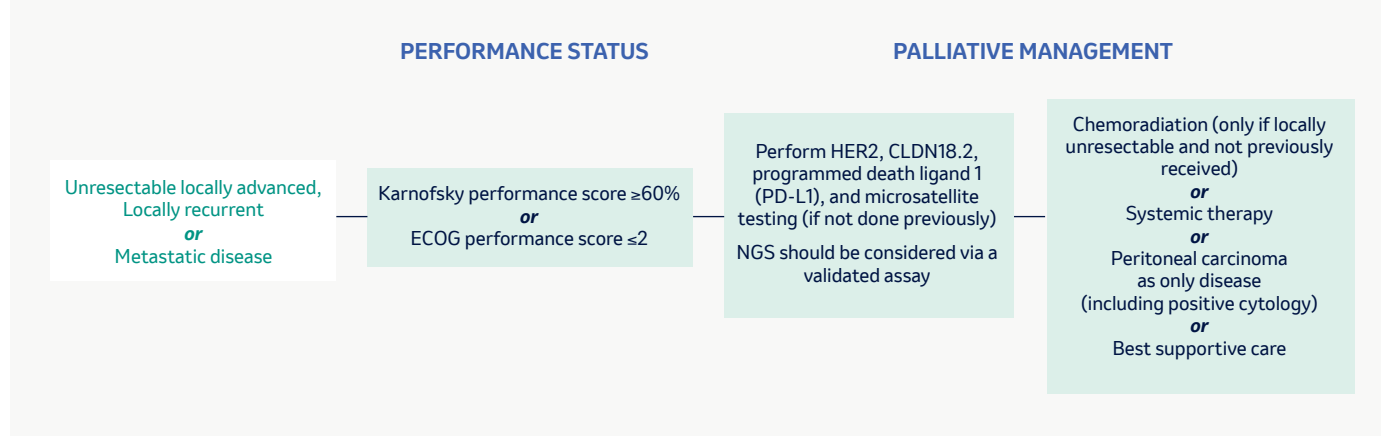
Esophageal/GEJ Cancer²

Biomarker	Disease stage	Testing methods
PD-L1	Newly diagnosed (any stage)	IHC
HER2 ^a	Metastatic adenocarcinoma ^{c,e}	IHC, ISH, FISH, NGS
CLDN18.2	Metastatic adenocarcinoma ^{c,e}	IHC
MSI ^b	Newly diagnosed (any stage)	PCR, NGS
MMR ^b	Newly diagnosed (any stage)	IHC

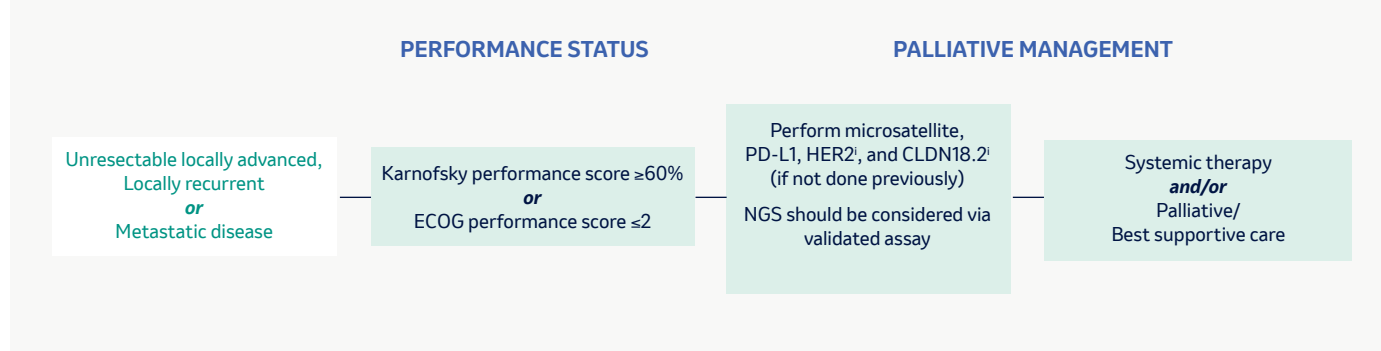
Colorectal Cancer^{3,4}

Biomarker	Disease stage	Testing methods
MSI ^f	Newly diagnosed (any stage)	PCR, NGS
MMR ^f	Newly diagnosed (any stage)	IHC
HER2	Metastatic ^c	IHC, FISH, NGS
RAS (KRAS/NRAS)	Metastatic ^c	NGS
BRAF	Metastatic ^c	NGS, IHC

NCCN Guidelines for Gastric Cancer^{1,9}



NCCN Guidelines for Esophageal and Esophagogastric Junction Cancers^{2,h}



^aThe NCCN Guidelines recommend that HER2 IHC be ordered/performed first, followed by ISH methods in cases showing 2+ (equivocal) expression by IHC. Positive (3+) or negative (0 or 1+) HER2 IHC results do not require further ISH testing. Cases with HER2:CEP17 ratio ≥ 2 or an average HER2 copy number ≥ 6.0 signals/cell are considered positive by ISH/FISH.

^bPCR/NGS for MSI and IHC for MMR proteins measure different biological effects caused by dMMR function.

^cMetastatic disease stage includes both documented as well as suspected cases.

^dTumor Epstein-Barr virus (EBV) status is emerging as a potential biomarker for personalized treatment strategies for gastric cancer, but is not currently recommended for clinical care. EBV testing should be performed if the morphology of the tumor contains prominent lymphoid stroma.

^eMetastatic disease stage includes both adenocarcinomas documented as well as suspected cases.

^fIHC for MMR and DNA analysis for MSI are different assays and measure different biological effects caused by dMMR function.

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ⁱHER2 and CLDN18.2 testing is specific to adenocarcinoma.

BRAF = v-raf murine sarcoma viral oncogene homolog B1; CEP17 = centromeric region of chromosome 17; CLDN18.2 = Claudin 18 isoform 2; dMMR = mismatch repair deficient; ECOG = Eastern Cooperative Oncology Group; FISH = fluorescence in situ hybridization; GEJ = gastroesophageal junction; HER2 = human epidermal growth factor receptor 2; IHC = immunohistochemistry; ISH = in situ hybridization; KRAS = Kristen rat sarcoma virus; MMR = mismatch repair; MSI = microsatellite instability; NGS = next-generation sequencing; NRAS = neuroblastoma rat sarcoma virus; PCR = polymerase chain reaction; PD-L1 = programmed death ligand 1; RAS = rat sarcoma virus.

References: 1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]) for Gastric Cancer V.3.2025. © National Comprehensive Cancer Network, Inc. 2025. All rights reserved. Accessed August 25, 2025. To view the most recent and complete version of the guideline, go online to NCCN.org. 2. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]) for Esophageal and Esophagogastric Junction Cancers V.4.2025. © National Comprehensive Cancer Network, Inc. 2025. All rights reserved. Accessed August 25, 2025. To view the most recent and complete version of the guideline, go online to NCCN.org. 3. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]) for Colon Cancer V.4.2025. © National Comprehensive Cancer Network, Inc. 2025. All rights reserved. Accessed July 1, 2025. To view the most recent and complete version of the guideline, go online to NCCN.org. 4. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]) for Rectal Cancer V.3.2025. National Comprehensive Cancer Network. Accessed September 25, 2025. To view the most recent and complete version of the guideline, go online to NCCN.org.



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