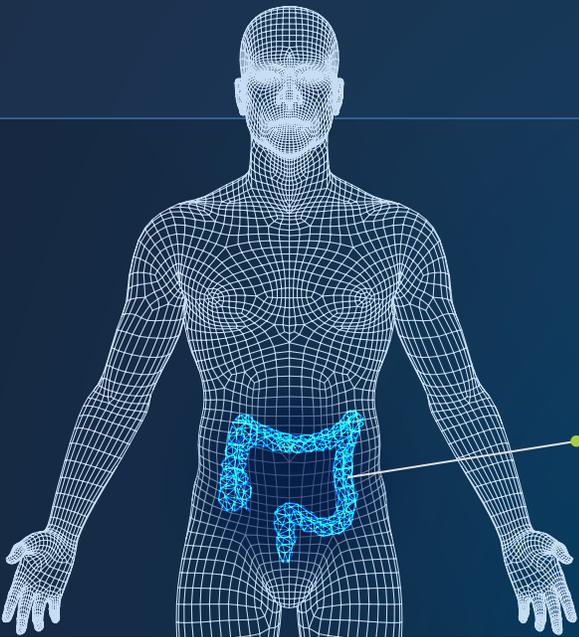


LATEST TESTING RECOMMENDATION

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]) recommend testing for HER2 amplification in patients with unresectable or metastatic colorectal cancer^{1,2*}



Prevalence of HER2 amplification in colorectal cancer

HER2 amplification is present in **~3% to 5% of all patients** with colorectal cancer^{1,3,4}

Prevalence is **higher in patients with RAS/BRAF WT tumors** (5% to 14%)¹

HER2 amplification testing can guide appropriate treatment decisions for patients with metastatic colorectal cancer (mCRC)^{1,2,5}

- The NCCN Guidelines[®] currently recommend HER2-targeted therapies as treatment options for HER2+ *RAS/BRAF* WT mCRC^{1,2}

*NCCN Guidelines state that if the tumor is already known to have a *KRAS/NRAS* or *BRAF* mutation, HER2 testing is not indicated.^{1,2}

HER = human epidermal growth factor receptor; NCCN = National Comprehensive Cancer Network; WT = wild type.

HER2 amplification testing can help identify patients who may benefit from a targeted treatment approach⁴

HER2 amplification is associated with poorer response and survival outcomes in patients treated with anti-EGFR agents^{6,7}

- Currently, anti-EGFR agents are a common treatment approach for *RAS/BRAF* WT mCRC in later lines of therapy^{5,7}
- However, HER2 amplification may be associated with decreased activity of anti-EGFR therapies in patients with *RAS/BRAF* WT mCRC^{6,7}

In a retrospective analysis of patients who were identified to have *RAS/BRAF* WT mCRC using NGS and received 2L or 3L anti-EGFR-based therapy^{7*}:



HR = 10.66 (95% CI: 4.5-25.1); P < 0.001

Including HER2 status assessment for all patients with mCRC may help inform treatment decisions

*This study compared PFS of HER2-amplified and non-HER2-amplified patients receiving anti-EGFR antibody treatment in 2 cohorts. HER2 amplification status was identified using ISH (cohort 1) and NGS (cohort 2). Results from cohort 2 are shown. In cohort 1, median PFS on anti-EGFR-based therapy was 2.8 months (95% CI: 1.8-3.8) in HER2-amplified patients compared with 8.1 months (95% CI: 5.8-10.3) in non-HER2-amplified patients. PFS on an anti-EGFR antibody-based regimen was significantly shorter among HER2-amplified patients compared with non-HER2-amplified patients (HR = 7.05 [95% CI: 3.4-14.9]; P < 0.001).⁷

2L = second line; CI = confidence interval; EGFR = epidermal growth factor receptor; HR = hazard ratio; ISH = in situ hybridization; NGS = next-generation sequencing; PFS = progression-free survival.

References: 1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]) for Colon Cancer V3.2022. © National Comprehensive Cancer Network, Inc. 2023. All rights reserved. Accessed February 21, 2023. To view the most recent and complete version of the guideline, go online to [NCCN.org](https://www.nccn.org). NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. 2. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]) for Rectal Cancer V4.2022. © National Comprehensive Cancer Network, Inc. 2023. All rights reserved. Accessed February 21, 2023. To view the most recent and complete version of the guideline, go online to [NCCN.org](https://www.nccn.org). NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. 3. Sartore-Bianchi A, Lonardi S, Martino C, et al. Pertuzumab and trastuzumab emtansine in patients with HER2-amplified metastatic colorectal cancer: the phase II HERACLES-B trial. *ESMO Open*. 2020;5(5):e000911. doi:10.1136/esmooopen-2020-000911 4. Ahcene Djabballah S, Daniel F, Milani A, Ricagno G, Lonardi S. HER2 in Colorectal Cancer: The Long and Winding Road From Negative Predictive Factor to Positive Actionable Target. *Am Soc Clin Oncol Educ Book*. 2022;42:1-14. doi:10.1200/EDBK.351354 5. Raghav KPS. The role of HER2 amplification testing in metastatic colorectal cancer. *Clin Adv Hematol Oncol*. 2018;16(11):720-722. 6. Sartore-Bianchi A, Amatu A, Porcu L, et al. HER2 positivity predicts unresponsiveness to EGFR-targeted treatment in metastatic colorectal cancer. *Oncologist*. 2019;24(10):1395-1402. 7. Raghav K, Loree JM, Morris JS, et al. Validation of HER2 amplification as a predictive biomarker for anti-epidermal growth factor receptor antibody therapy in metastatic colorectal cancer. *JCO Precis Oncol*. 2019. doi:10.1200/PO.18.00226

