Know Your Biomarker

RAF | CEA | ctDNA | DPYD | FAP | HER2 | KRAS | Lyn

# Tumor Location / Sidedness

MSI | MSS | N

NRAS | NTRK Fusion | PIK3CA | RET | TMB | UGT1A1

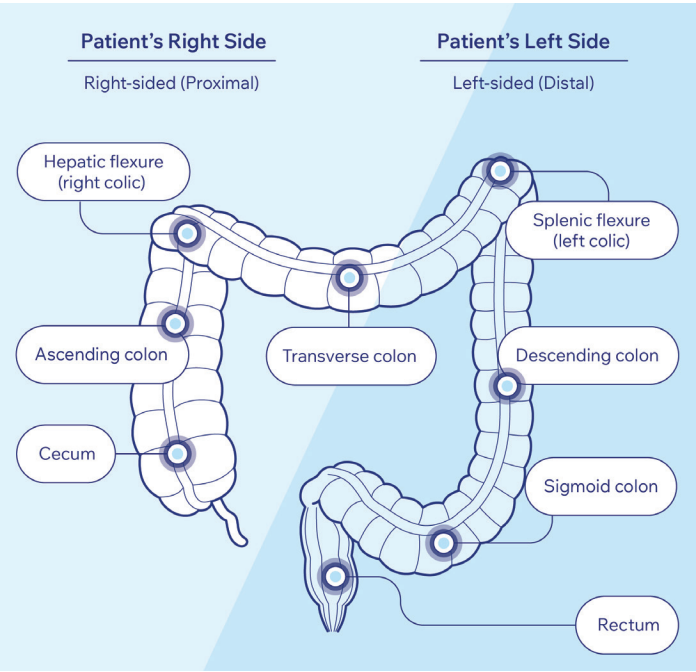
**Who should have tumor location / sidedness biomarker testing?**

Tumor (tumour) location should be determined for all colorectal cancer (bowel cancer) patients at diagnosis.

**What is tumor location / sidedness?**

The large intestine (bowel) is made up of 6 segments, cecum (caecum), ascending colon, transverse colon, descending colon, sigmoid colon, and rectum. The hepatic flexure (right colic flexure) is the turning point between the ascending colon and transverse colon. The splenic flexure (left colic flexure) is the turning point between the transverse colon and descending colon. Colorectal cancer can develop in any of these locations.

Often, colorectal cancer is referred to as “right sided” or “left sided”. This is the “sidedness” of the tumor. Right-sided tumors, also known as proximal tumors, are located in the cecum, ascending colon, hepatic flexure, or the first two-thirds of the transverse colon. Left-sided tumors, also called distal tumors, are located in the last third of the transverse colon, splenic flexure, descending colon, sigmoid colon, or rectum.




| Right-Sided / Proximal | Left-Sided / Distal |
|---|---|
| Less common than left-sided | More common than right-sided |
| More common in women | More common in men |
| More common in older patients | More common in younger patients |
| More likely in patients with Lynch Syndrome | More likely in patients with Familial Adenomatous Polyposis (FAP) |
| More likely to have:<br>→ MSI-High / dMMR<br>→ KRAS mutations<br>→ BRAF mutations | More likely to have:<br>→ HER2 amplification |
| Likely symptoms:<br>→ anemia<br>→ bleeding | Likely symptoms:<br>→ constipation<br>→ change in bowel habits |
| More often flat shaped (more likely to go unnoticed until quite large) | More often polyp shaped (more likely to be noticed, even when small) |
| Usually diagnosed at later stage | Usually diagnosed at earlier stage |
| More likely to be in the mucinous type subgroup of adenocarcinomas | More likely to be in the tubular or villous type adenocarcinoma subgroups |
| More likely to spread to the abdominal lining (peritoneum), rather than liver and lung | More likely to spread to liver and lung, rather than abdominal lining (peritoneum) |
| Less likely to respond well to EGFR inhibitors (even when KRAS/NRAS/BRAF wild-type) | More likely to respond well to EGFR inhibitors |

Several factors likely contribute to the differences in right-sided and left-sided colorectal cancers.

→ The right and left sides of the colon develop from two different parts of the embryo, the midgut and the hindgut.

→ As digested food travels through the large intestine, the right and left sides are exposed to different nutrients and digestive substances, such as bile acids.

→ The populations of normal gut bacteria (intestinal microbiome) that live in the large intestine vary between right and left side. An increasing number of studies suggest that gut bacteria is related to colorectal cancer development.

**How is tumor location / sidedness tested? How are the results reported?**

The location of your colorectal cancer may be identified in several ways. It may be described in imaging reports (CT scan, X-ray, PET scan, MRI scan), in reports from surgical procedures (colonoscopy, colectomy), or in pathology reports (biopsy results). Tumor location may be reported as the specific location (for example splenic flexure, sigmoid colon, rectum), as "right-sided" or "left-sided", or as "proximal" or "distal".

**What do my tumor location / sidedness results mean for me? How do they impact my treatment?**

**If your colorectal cancer is right-sided**

→ Right-sided colon cancer has a better prognosis at early stages (I and II).

→ Immunotherapy is effective against right-sided colorectal cancer.

→ Bevacizumab added to traditional chemotherapy is more effective than EGFR inhibitors with traditional chemotherapy.

→ Surgical treatment of fight-sided colon cancer may involve removal of your cecum, ascending colon and/or a part of the transverse colon.

**If your colorectal tumor is left-sided**

→ Left-sided colorectal cancer has a better prognosis at later stages (III and IV / metastatic).

→ Adjuvant chemotherapy with 5-FU based regimens is effective against left-sided colorectal cancer.

→ Traditional chemotherapy combined with EGFR inhibitors, such as cetuximab or panitumumab, is more effective than chemotherapy plus bevacizumab.

→ Surgical treatment of left-sided colon cancer may involve having part of your transverse, descending, and/or sigmoid colon removed. If your cancer is low in the sigmoid colon, you may also have part of your rectum removed. If your cancer originates in the rectum, you will have some or all of your rectum removed.

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Biomarker testing can give you and your medical team valuable knowledge about your cancer and help guide your treatment choices. For more information about colorectal cancer biomarkers, please visit knowyourbiomarker.org and talk to your medical team.