Common Biomarkers in Stomach Cancer

- **HER2**: HER2 positive tumors have above normal HER2 protein, which causes cancer cells to grow. Learn more.
- **MSI-high and dMMR**: When cells lose their ability to correct DNA errors, those cells can replicate uncontrollably, and cause cancer. Learn more
- **PD-L1**: Cells having an abnormally high amount of the PD-L1 protein allow gastric cancer cells to evade the immune system. Learn more.
- **TMB:** Tumors with more than one mutation have a high tumor mutational burden (TMB). Learn more.
- **EBV:** Epstein-Barr virus may play a role in transforming normal stomach cells into cancerous ones. Learn more.
- **Tumor-agnostic biomarkers**: Some biomarkers such as NTRK, BRAF mutations and RET fusions are not specific to stomach cancer. Learn more
- **Emerging biomarkers:** As new biomarkers are identified and researched, more individualized treatment will become available. Learn more about CLDN18.2, FGFR, MUC17, KRAS and DKK1.

Biomarkers can play a crucial role in tailoring targeted therapies and personalized treatment plans for stomach cancer patients. While new biomarkers are being discovered at a rapid rate, those listed below are among the most common biomarkers impacting stomach cancer treatment right now.

- **HER2** (Human Epidermal Growth Factor Receptor 2): The HER2 gene makes HER2 proteins, which can make cancer grow. When stomach cancer cells contain a higher-than-normal amount of the HER2 protein, they can grow more quickly and spread to other parts of the body. These tumors can be treated with targeted antibody drugs.
- **MSI-high and dMMR** (Microsatellite instability high and mismatch repair deficiency): MSI-H or dMMR are not exactly the same thing, but are interrelated. The Mismatch Repair System is responsible for correcting errors that occur during DNA replication. It identifies and fixes mismatches or small loops of DNA called microsatellites. When the dMMR biomarker is present, it means the MMR system is broken, and can cause a high rate of genetic mutations in microsatellite regions. When someone is MSI-high, it means their DNA is prone to mutations. These biomarkers may be responsive to immunotherapy such as keytruda.

- **PD-L1** (Programmed Death-Ligand-1): If tumor cells contain abnormally high amounts of a protein called PD-L1, targeted drugs such as nivolumab (Opdivo) and pembrolizumab (Keytruda) can be used to prevent the suppression of T cells and free up the immune system to fight the cancer.
- **TMB:** (Tumor mutational burden): If cancer cells have more than one gene mutation, they are said to have a high TMB, which means they have a higher chance of responding to immunotherapy checkpoint inhibitors such as the drug pembrolizumab (Keytruda).
- **EBV:** Epstein-Barr virus may play a role in transforming normal stomach cells into cancerous ones.
- **Tumor-agnostic biomarkers**: Tumor-agnostic biomarkers are molecular characteristics that are related to many different types of cancer, including stomach cancer. These biomarkers, such as NTRK (Neurotrophic Tyrosine Receptor Kinase), BRAF mutations and RET fusion, are not limited to a specific organ or tissue, and are increasingly important in guiding targeted therapies for a variety of cancers, including stomach cancer. For example, while rare, NTRK tumors respond well to targeted therapy such as larotrectinib (Vitrakvi) and entrectinib (Rozlytrek).

What are emerging biomarkers, and why are they important?

Emerging biomarkers are biomarkers not yet widely established, but ongoing research suggests they have the potential to impact treatment plans and outcomes. There are a number of emerging stomach cancer biomarkers already beginning to factor into treatment plans, and patients may want to research and ask their care team about them.

- **CLDN 18.2** (Claudin 18.2): Claudins are proteins that help control how molecules flow between cells. Claudin 18.2 is found in the stomach lining, and higher-than-normal levels of it are associated with stomach cancer. While research into Claudin 18.2 and stomach cancer is ongoing, there is reason to be optimistic about the use of monoclonal antibodies as a targeted therapy.
- **FGFR2b** (Fibroblast growth factor receptor 2b): The FGFR2 gene provides instructions for making a protein involved in the regulation of cell growth and division. FGFR2b is a "splice variant" or unusual form of FGFR2 that is associated with many diseases and disorders. FGFR2b is being explored as a biomarker for stomach cancer which could be targeted with antibodies in combination with chemotherapy.
- **MUC17** (Mucin 17): Mucins are proteins that exist within a thin wall of skin that produces stomach-protecting mucous. MUC17 is found in higher-than-normal amounts in around half of gastric cancers, and a clinical trial exploring an immunotherapy called AMG 199 in treatment of MUC17-positive stomach cancer was recently concluded.
- **KRAS** (Kirsten rat sarcoma viral oncogene homolog): The KRAS gene determines the development of the KRAS protein, which helps control cell growth and division. A variant form of KRAS, which can cause uncontrolled cell growth and contribute to cancer development, can sometimes be found in many types of cancer, including stomach cancer.
- **DKK1** (Dickkopf-1): The DKK1 protein helps regulate cell growth and development. An elevated DKK1 level is associated with stomach cancer, as well as other cancers.