Why Getting Personal Can Be Lifesaving?

Metastatic Colorectal Cancer Biomarkers and Treatment Impacts

As science evolves, new biomarkers are emerging as possible targets for drug developments and treatment design.

BIOMARKER (in alphabetical order)	WHAT IS THE TREATMENT IMPACT?
BRAF	• The current standard therapies for first-line treatment of BRAF-mutated mCRC are chemotherapy (5-fluorouracil, leucovorin, oxaliplatin, and irinotecan) with or without anti-angiogenic agents in patients with good performance status. • Tumours with a BRAF V600E mutation, who have received prior systemic therapy, can be treated with encorafenib in combination with cetuximab. • Tumours without BRAF mutation (wild-type) are typically treated with EGFR inhibitors.
HER	• HER2 amplification and overexpression are predictive biomarkers for poor response to treatment with EGFR inhibitors • HER2 negative tumours are treated based on the other patient and biomarker information. • Based on recent evidence, they might benefit from anti-HER 2 treatment. It is recommended to consider clinical trials.
KRAS	• Tumours without KRAS mutation (wild-type) are treated with EGFR inhibitors (cetuximab and panitumumab). • Tumours with KRAS mutations are unlikely to respond to EGFR inhibitors and are usually treated with traditional chemotherapy with or antiangiogenic agents.
MSI	• HER2 amplification and overexpression are predictive biomarkers for poor response to treatment with EGFR inhibitors • HER2 negative tumours are treated based on the other patient and biomarker information. • Based on recent evidence, they might benefit from anti-HER 2 treatment, It is recommended to consider clinical trials.
MSI	• Has strong predictive value for the use of immune checkpoint inhibitors.

NRAS	• Tumours without NRAS mutation (wild type) are treated with EGFR inhibitors (cetuximab and panitumumab). • Tumours with NRAS mutations are unlikely to respond to EGFR inhibitors therefore are treated with traditional chemotherapy with or without antiangiogenic agents.
HER	• Tumours presenting an NTRK fusion protein can be treated with TRK inhibitors, such as larotrectinib and entrectinib. • Colorectal cancer with NTRK mutation is treated with traditional chemotherapy with or without antiangiogenic agents or anti-EGFR if RAS/BRAF are not mutated
SIDENESS	• For the development of effective therapy regimes and better treatment options, it is essential to evaluate right-sided and left-sided tumours as separate entities and design the therapy regime considering the differences between these tumours. • Right-sided tumours, with RAS/BRAF wild-type status, have a worse prognosis and limited response anti EGFR treatment. it is recommended to use as first-line chemotherapy with antiangiogenic agents. • Left-sided tumours usually have a better prognosis and show a better response anti EGFR treatment. it is recommended to use as first-line chemotherapy with anti-EGFR agents.
DPYD	• In patients with DPYD mutation associated with partial DPD enzyme deficiency, doses of fluorouracil (5-FU) related drugs may be reduced to lower the risk of severe toxic effects. • In patients with DPYD mutation associated with total DPD enzyme deficiency, avoiding fluorouracil (5-FU) related drugs is strongly suggested.
RAS	• Tumours without NRAS mutation (wild-type) are treated with EGFR inhibitors (erlotinib, gefitinib, cetuximab, necitumumab). • CRC tumours with NRAS mutations are unlikely to respond to EGFR inhibitors therefore are treated with traditional chemotherapy with or without antiangiogenic agents.

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