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Qamra and colleagues characterized epigenetic promoter alterations in gastric cancer and identified unaltered promoters, somatic tumor-specific promoters gained in tumors, and normal-specific promoters lost in tumors. Overall, 18% of the gastric cancer somatic promoters were alternative promoters that resulted in overexpression of alternative transcript isoforms as well as proteins with altered N-terminal peptide sequences, which may allow for increased proteomic diversity in gastric cancer. Further, alternative somatic promoter usage was linked to decreased tumor immunity. The N-terminal peptides downregulated by gastric cancer somatic promoters elicited immune responses, suggesting that the tumor-specific promoters may decrease tumor immunogenicity. Altogether, these findings identify tumor-specific alternative promoters in gastric cancer that may produce tumor-specific isoforms to promote tumor immune evasion. For details, please see the article by Qamra and colleagues on page 630.

Precis:

A Phase Ib Dose-Escalation Study of Encorafenib and Cetuximab with or without Alpelisib in Metastatic BRAF-Mutant Colorectal Cancer .............. 610

Precis: The RAF inhibitor encorafenib in combination with the EGFR inhibitor cetuximab is tolerable and achieves responses in patients with BRAF-mutant colorectal cancer with or without PI3Kα inhibition with alpelisib.

See commentary, p. 558

Phase I, Dose-Escalation, Two-Part Trial of the PARP Inhibitor Talazoparib in Patients with Advanced Germline BRCA1/2 Mutations and Selected Sporadic Cancers ..................... 620

Precis: The PARP inhibitor talazoparib is well tolerated and has single-agent antitumor activity in patients with breast or ovarian cancer harboring germline BRCA1/2 mutations, and in patients with pancreatic or lung cancer.

Epigenomic Promoter Alterations Amplify Gene Isoform and Immune Diverse in Gastric Adenocarcinoma ......................... 630

Precis: Characterization of epigenetic promoter alterations in gastric cancer reveals that alternative promoters upregulate tumor-specific oncogenic isoforms and downregulate immunogenic peptides.