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### VIEWS

**In The Spotlight**

**Quantifying the Benefits of Genome-Driven Oncology**

A.M. Schram and D.M. Hyman

See article, p. 586

**Toward Molecularly Driven Precision Medicine in Lung Adenocarcinoma**

D. Liu, N.I. Vokes, and E.M. Van Allen

See article, p. 596

**Targeting BRAF-Mutant Colorectal Cancer: Progress in Combination Strategies**

R. Sundar, D.S. Hong, S. Kopetz, and T.A. Yap

See article, p. 610

### REVIEW

**Neoadjuvant Trials in ER+ Breast Cancer: A Tool for Acceleration of Drug Development and Discovery**

A.L. Guerrero-Zotano and C.L. Arteaga

### RESEARCH BRIEF

**An Acquired HER2T798I Gatekeeper Mutation Induces Resistance to Neratinib in a Patient with HER2 Mutant-Driven Breast Cancer**


Précis: A patient with breast cancer with an activating HER2T886 protakope mutation who initially responded to neratinib acquired a HER2T798I mutation that promoted neratinib resistance, but may retain sensitivity to afatinib.

### RESEARCH ARTICLES

**High-Throughput Genomics and Clinical Outcome in Hard-to-Treat Advanced Cancers: Results of the MOSCATO 01 Trial**


Précis: In a prospective clinical trial of patients with advanced solid tumors, genomics analyses identified genomic alteration-matched therapies that extended progression-free survival in 33% of patients.

See commentary, p. 552

**Prospective Comprehensive Molecular Characterization of Lung Adenocarcinomas for Efficient Patient Matching to Approved and Emerging Therapies**

On the 

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\( \alpha \) colorectal cancer with or without PI3K inhibition in patients with advanced lung adenocarcinoma, allowing for selection of clinically beneficial matched targeted therapies. 

See commentary, p. 555

A Phase Ib Dose-Escalation Study of Encorafenib and Cetuximab with or without Alpelisib in Metastatic 

BRAF-Mutant Colorectal Cancer ...... 610


Précis: 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 PI3K\( \alpha \) 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


Précis: 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 Immunogenic Diversity in Gastric Adenocarcinoma ............... 630


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

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.