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Genomics of Ovarian Cancer Progression Reveals Diverse Metastatic Trajectories Including Intraepithelial Metastasis to the Fallopian Tube .................. 1342
Précis: Multisite sequencing of high-grade serous ovarian cancers highlights genomic instability as an early event in disease progression and identifies a subset of serous tubal intraepithelial carcinomas as metastases rather than precursor lesions.
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Oncogenic MET as an Effective Therapeutic Target in Non–Small Cell Lung Cancer Resistant to EGFR Inhibitors: The Rise of the Phoenix

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Culprit or Bystander? The Role of the Fallopian Tube in “Ovarian” High-Grade Serous Carcinoma

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Making the Most of Cancer Surgery with Neoadjuvant Immunotherapy

I. Melero, P. Berraondo, M.E. Rodriguez-Ruiz, and J.L. Pérez-Gracia
See article, p. 1382
Phase IB Study of Vemurafenib in Combination with Irinotecan and Cetuximab in Patients with Metastatic Colorectal Cancer with BRAFV600E Mutation


Précis: Vemurafenib plus irinotecan and cetuximab was generally well tolerated and achieved a 35% response rate in patients with BRAFV600E metastatic colorectal cancer, and responses correlated with BRAFV600E cfDNA levels.

TGFβ1-Mediated SMAD3 Enhances PD-1 Expression on Antigen-Specific T Cells in Cancer


Précis: TGFβ1 promotes a SMAD3-dependent increase in PD-1 expression on TILs, suppressing antitumor immunity and increasing tumor growth in vivo.

Improved Efficacy of Neoadjuvant Compared to Adjuvant Immunotherapy to Eradicate Metastatic Disease


Précis: Neoadjuvant immunotherapy extends survival and reduces metastatic disease more effectively than adjuvant immunotherapy in mouse models of metastatic triple-negative breast cancer. See commentary, p. 1312

Acknowledgment to Reviewers

Correction

Correction: Molecular Heterogeneity and Receptor Coamplification Drive Resistance to Targeted Therapy in MET-Amplified Esophagogastric Cancer

Bakh and colleagues report the case of a patient with recurrent non–small cell lung cancer (NSCLC) harboring an EGFR exon 19 deletion mutation and high-level MET amplification who initially responded to a type I MET inhibitor combined with an EGFR inhibitor but acquired a METD1228V mutation that promoted resistance. Protein modeling predicted that METD1228V would not alter sensitivity to type II MET inhibitors, which bind the inactive conformation of MET. Consequently, the patient was treated with a type II MET inhibitor combined with an EGFR inhibitor and achieved an ongoing response. These results indicate that MET may be therapeutically targeted in NSCLC, and type II MET inhibitor sensitivity may be maintained even in cells resistant to type I MET inhibitors. Therefore, determining MET inhibitor resistance mechanisms may guide drug selection in patients. For details, please see the article by Bakh and colleagues on page 1334.