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For more News and Research Watch, visit Cancer Discovery online at http://CDnews.aacrjournals.org.

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RESEARCH ARTICLES

First-in-Humans Trial of an RNA Interference Therapeutic Targeting VEGF and KSP in Cancer Patients with Liver Involvement 406
Précis: A lipid nanoparticle multitarget siRNA formulation is deliverable to tumors and shows evidence of on-target activity in patients with advanced cancers enrolled in a phase I trial.

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Colorectal Cancer: Looking for Answers in the Microbiota 384
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The Basic Principles of Chimeric Antigen Receptor Design 388
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Biallelic Deleterious BRCA1 Mutations in a Woman with Early-Onset Ovarian Cancer 399
Précis: The presence of a dysfunctional BRCA1 BRCT domain variant in trans with a known deleterious BRCA1 mutation was documented in a woman with early-onset ovarian carcinoma.
See commentary, p. 376

Précis
For more News and Research Watch, visit Cancer Discovery online at http://CDnews.aacrjournals.org.
Multifunctional T-cell Analyses to Study Response and Progression in Adoptive Cell Transfer Immunotherapy .............. 418
Précis: Single-cell immune monitoring of patients receiving adoptive cell transfer therapy reveals time-dependent changes in adoptively transferred and endogenous T-cell functionality. See commentary, p. 379

Targeted Inhibition of the Molecular Chaperone Hsp90 Overcomes ALK Inhibitor Resistance in Non-Small Cell Lung Cancer ................. 430
Précis: Inhibition of HSP90 with ganetespib may represent an alternative or complementary therapeutic strategy for treatment of ALK-positive non-small cell lung cancer.

RHOA-FAK Is a Required Signaling Axis for the Maintenance of KRAS-Driven Lung Adenocarcinomas .................. 444
Précis: RHOA-FAK signaling is a genotype-specific therapeutic target in aggressive KRAS-mutant, INK4A/ARF-deficient non-small cell lung cancers.

Primary Melanoma of the CNS in Children Is Driven by Congenital Expression of Oncogenic NRAS in Melanocytes ..... 458
Précis: Early embryonic NRAS mutation promotes melanocyte proliferation and induces early-onset primary melanoma of the central nervous system but not cutaneous melanoma. See commentary, p. 382

For more News and Research Watch, visit Cancer Discovery online at http://CDnews.aacrjournals.org. Online-only News stories include the following:

- Drug Combo Effective Against Pancreatic Cancer
- Reprioritizing Cancer Clinical Studies
- Glycoengineered Antibodies Show Promise

- FDA Approves Stivarga for GIST
- Analyses Suggest Risks with mTOR Inhibitors
- Ramucirumbo Aids Gastric Cancer Survival

Tabernero and colleagues report the results of a phase I dose-escalation and expansion study assessing the safety, activity, and pharmacodynamics of ALN-VSP, a lipid nanoparticle containing siRNAs against vascular endothelial growth factor A (VEGFA) and kinesin spindle protein (KSP), in patients with advanced solid tumors with liver involvement. One patient with metastatic endometrial cancer had a complete response and 3 patients (2 with metastatic renal cell carcinoma and 1 with metastatic pancreatic neuroendocrine tumor) experienced disease stabilization. Post-treatment tumor biopsies showed evidence of intratumoral delivery, increased VEGFA mRNA cleavage, and decreased VEGFA and KSP mRNA levels compared with pre-treatment biopsy samples, consistent with an on-target response and an RNAi mechanism of action. For details, please see the article by Tabernero and colleagues on page 406.