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Advances in the Treatment of Acute Myeloid Leukemia: New Drugs and New Challenges .............. 506
N.J. Short, M. Konopleva, T.M. Kadia, G. Borthakur, F. Ravandi, C.D. Dinardo, and N. Daver

## RESEARCH ARTICLES
**Characteristics and Outcome of AKT1E17K-Mutant Breast Cancer Defined through AACR Project GENIE, a Clinicogenomic Registry** .................................. 526
Précis: Data from AACR Project GENIE were used to investigate the effects of the rare AKT1E17K mutation in ER+ breast cancer, showing the challenges and advantages of using this type of real-world evidence.

See commentary, p. 490

**Monocytic Subclones Confer Resistance to Venetoclax-Based Therapy in Patients with Acute Myeloid Leukemia** .................................. 536
Précis: Compared with less differentiated acute myeloid leukemia (AML), monocytic AML is more resistant to venetoclax-based therapy, a phenomenon that may be attributable to dedifferentiation of preexisting monocytic subclones.
Impaired Death Receptor Signaling in Leukemia Causes Antigen-Independent Resistance by Inducing CAR T-cell Dysfunction ............... 552


Précis: Response to CD19-directed CAR T cells in acute lymphoblastic leukemia was dependent on death receptor signaling, and exposure to ALL cells with impaired death receptor signaling caused CAR T cells to adopt an exhausted-like phenotype.

See commentary, p. 492

Relapse-Fated Latent Diagnosis Subclones in Acute B Lineage Leukemia Are Drug Tolerant and Possess Distinct Metabolic Programs ............... 568


Précis: Minor subclones that are present at the time of diagnosis in B-progenitor acute lymphoblastic leukemia can cause relapse and exhibit distinct traits, including chemotherapy resistance, prior to treatment.

MYC Instructs and Maintains Pancreatic Adenocarcinoma Phenotype ............... 588


Précis: In a mouse model of mutant Kras-driven pancreatic ductal adenocarcinoma (PDAC), Myc activation was required for progression to PDAC, whereas Myc deactivation caused rapid regression of even established PDACs.

See commentary, p. 495

Oncogenic KRAS-Driven Metabolic Reprogramming in Pancreatic Cancer Cells Utilizes Cytokines from the Tumor Microenvironment ............... 608


Précis: In models of mutant Kras-driven pancreatic cancer, T2 cells in the tumor microenvironment produced the cytokines IL4 and IL13, which promoted metabolic reprogramming and tumorigenesis.