Clinical Cancer Research

Highlights

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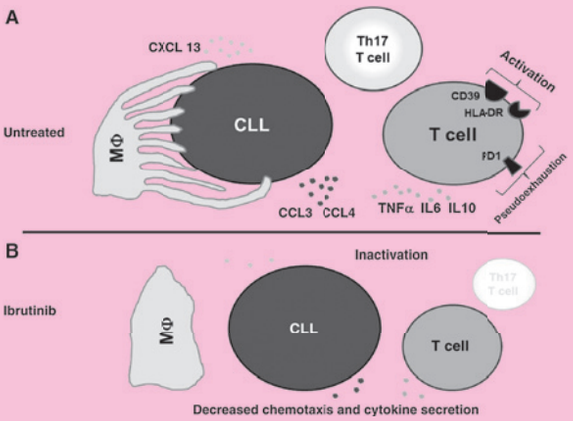
Selected Articles from This Issue



Ibrutinib Disrupts CLL Tumor-Microenvironment Interactions

Niemann *et al.* **Page 1572**

Niemann and colleagues describe global changes in the CLL microenvironment during treatment with the BTK inhibitor ibrutinib. They report on changes in cytokines and chemoattractants, T-cell subsets, and activation and demonstrate disruption of tumor-macrophage interactions in the bone marrow microenvironment. This work highlights the potent effects ibrutinib exerts on both the CLL cell and the tumor-microenvironment abating the chronic inflammatory drive in this disease. Mapping of the "new" tumor-microenvironment in patients on ibrutinib may inform the design of future clinical trials.

Core Patient-Reported Outcomes in Cancer Clinical Trials

Kluetz *et al.* **Page 1553**

The FDA's Office of Hematology and Oncology Products provide their perspective on patient-reported outcome (PRO) assessment in cancer trials. The authors describe existing PRO strategies and discuss new instruments that are becoming available. They consider focusing key PRO analyses on separate measures of symptomatic adverse events, physical function, and disease-related symptoms that are important contributors to health-related quality of life. Increased rigor in PRO measurement and trial conduct are necessary, and collaboration is needed to review new and existing tools to develop a PRO strategy suitable for the needs of all those who rely on PRO to inform treatment and policy decisions.

Personalized therapies in BRAF inhibitor resistant PDX

Krepler *et al.* **Page 1592**

Krepler and colleagues analyzed patient-derived xenografts established from melanoma patients relapsed on BRAF inhibitor therapy for possible mechanisms of resistance on the genomic and protein signaling levels. By combining these two data sets, they found that, while most tumors had reactivated the BRAF pathway, a subset had also activated PI3K or MET signaling as alternative drivers. Subsequently, the PDX were expanded under chronic BRAF inhibitor drug pressure, and rational second line combination therapies targeting the escape mechanisms were shown to be effective in preclinical *in vivo* trials.

Nuclear Export Inhibition and Radiation in Rectal Cancer

Ferreiro-Neira *et al.* **Page 1663**

XPO1 mediates the nuclear export of critical proteins required for rectal cancer proliferation and radiation resistance. Ferreiro-Neira and colleagues evaluated the radiosensitizing effects of XPO1 inhibitor (selinexor) in preclinical models of rectal cancer. Selinexor was tested in combination with radiation fractions similar to that given in clinical practice. Combined treatment promoted nuclear survivin accumulation and subsequent depletion, resulting in increased apoptosis and enhanced radiation antitumoral effects. These findings provide a novel therapeutic option for improving radiation sensitivity in the setting of rectal cancer.

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