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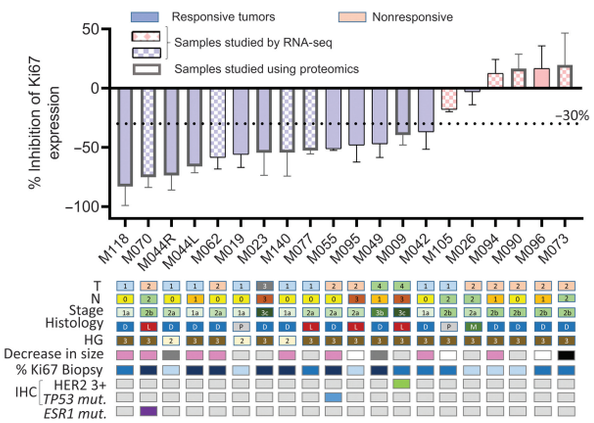
CLINICAL CANCER RESEARCH HIGHLIGHTS

Selected Articles from This Issue

Mifepristone Treatment in Breast Cancer Patients



Elía *et al.* | Page 866

Elía and colleagues propose that progesterone receptor (PR) ligands may serve as therapeutic tools for luminal breast cancer. Preclinical data suggest that antiprogestins inhibit tumor growth and metastasis in breast cancer models with higher levels of PR isoform A (PRA) than isoform B (PRA-H tumors), while they stimulate the metastatic burden in those with the opposite ratio. The MIPRA trial showed that mifepristone neoadjuvant treatment benefits patients with PRAH tumors and underscores the relevance of testing the PR isoform ratio before administering antiprogestins to patients with breast cancer. Proteomics, coupled with RNA-Seq profiling, revealed mifepristone-modulated biological processes that explain and strengthen the Ki67 data. The fact that lymph node metastases retain the PRA/PRB ratio as the primary tumor posits this subgroup of patients as recipients of antiprogestin treatment, even in adjuvant settings. These findings suggest that mifepristone may be included in the armamentarium against breast cancer in the future.

mCRC Treatment Response Evaluation by cfDNA and Matched WBCs

van 't Erve *et al.* | Page 899

Identification of tumor-specific mutations in cell-free DNA (cfDNA) for cancer detection, characterization, and monitoring can be confounded by germline and clonal hematopoiesis associated alterations, which have often required tumor tissue-guided approaches. van 't Erve and colleagues explored the clinical potential of combined ultra-deep sequencing of cfDNA and patient-matched white blood cell DNA for treatment response monitoring in patients with metastatic colorectal cancer. This tumor tissue-independent approach proved to be both essential and sufficient to eliminate these confounding alterations and, with a single blood draw, makes liquid biopsy circulating tumor DNA testing widely accessible to cancer patients.

Radiation Therapy and the Immune System

Cheema *et al.* | Page 921

Radiation therapy (RT) is frequently used as a curative modality for the treatment of human cancers. Clinical responses to tumor damaging ionizing radiations include anti-tumor immune activation. Here, Cheema and colleagues show the sequence of molecular interactions and cellular crosstalk underlying the cell cycle disruption, activation of the DNA damage response, and stimulation of innate immunity in plasma obtained from patients treated with radiation therapy for prostate cancer. Insight into the sequence and timing of these systemic events inform strategies for improvement of immunotherapy in combination with RT-based cancer treatments.

Crizotinib in Myeloproliferative Neoplasms

Gurska *et al.* | Page 943

Philadelphia-negative myeloproliferative neoplasms (MPN), which are characterized by JAK/STAT pathway activation, have persistence mechanisms which lead to loss of response to JAK inhibitors. Gurska and colleagues demonstrate preclinical efficacy of the inhibitor crizotinib in MPN in inhibiting proliferation and JAK/STAT signaling in MPN patient cells and cell lines. The authors found that the crizotinib target RON kinase interacts with JAK2 in JAK inhibitor persistent cells, and that treatment with crizotinib overcomes JAK inhibitor resistance by disrupting this interaction. This work suggests that crizotinib should be investigated for the treatment of MPN patients, particularly in the setting of JAK inhibitor resistance.

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