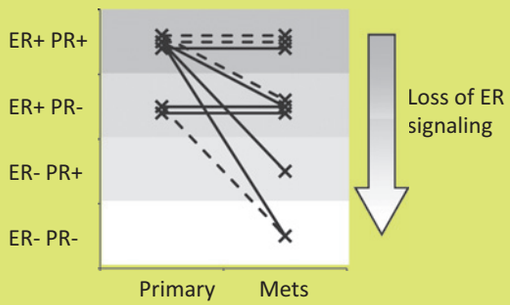
Clinical Cancer Research

Highlights

June 1, 2016 • Volume 22 • Number 11

Selected Articles from This Issue



Dynamic ER Adaptation to AI Therapy

Varešlija *et al.* Page 2765

Resistance to aromatase inhibitors (AIs) is an ongoing clinical challenge in the treatment of breast cancer. To investigate the role of the estrogen receptor in AI resistance, Varešlija and colleagues conducted global ChIP-sequencing analysis in AI-resistant breast cancer cells and profiled patient tumor samples before, during, and after AI therapy. The estrogen receptor rapidly adapted to AI therapy, developing estrogen-independent transcriptional activity; however, during later stages of resistant disease progression, activity and even expression of the estrogen receptor was frequently lost. This study highlights the need to reassess tumor status during disease progression.

Prostate Cancer Correlation of RSI-MRI and Gleason Grade

Yamin *et al.* Page 2668

Current multiparametric magnetic resonance imaging (MP-MRI) techniques for detecting prostate cancer are limited regarding tumor conspicuity assessment, *in vivo* characterization, and localization. Yamin and colleagues demonstrated that restriction spectrum imaging (RSI-MRI), a novel diffusion-based technique, differentiates among benign, low-grade, and high-grade prostate cancer within tumors. The RSI-MRI cellularity index used in this study may help to improve and refine diagnosis and staging of prostate cancer. Additionally, because it can detect intratumor variation, RSI-MRI may facilitate the targeting of most aggressive portions of tumors with interventions such as focal radiotherapy, magnetic resonance (MR)-guided focused ultrasound surgery, and MR-guided targeted biopsy.

Preclinical Study of Evofosfamide and Topotecan

Zhang *et al.* Page 2697

Tumor cells residing in tumor hypoxic zones are a major cause of drug resistance and tumor relapse. Targeting tumor hypoxia may improve cancer therapy and should be integrated in personalized medicine strategies. Zhang and colleagues investigated the efficacy of evofosfamide, a hypoxia-activated prodrug, and its combination with topotecan in neuroblastoma and rhabdomyosarcoma preclinical models. They demonstrated that targeting tumor hypoxia with evofosfamide improves antitumor effects of topotecan, including tumor growth inhibition, delayed tumor relapse, and enhanced animal survival in preclinical tumor models, which provides a new therapeutic approach for the treatment of pediatric solid tumors.

Antiangiogenic Activity and Toxicity of Itraconazole Isomers

Shim *et al.* Page 2709

The antifungal drug itraconazole has been found to possess potent antiangiogenic and anti-hedgehog activity. A major limitation of itraconazole, however, is its hepatotoxicity. In this study, each of the four stereoisomers of itraconazole was separated and assessed for their antiangiogenic activity and hepatotoxicity. It was found that one of the four stereoisomers possesses slightly higher antiangiogenic and anticancer activity without significantly decreased hepatotoxicity, making the specific stereoisomer an attractive candidate for development as a novel antiangiogenic and anticancer drug.

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Clin Cancer Res 2016;22:2597.