Clinical Cancer Research

Highlights

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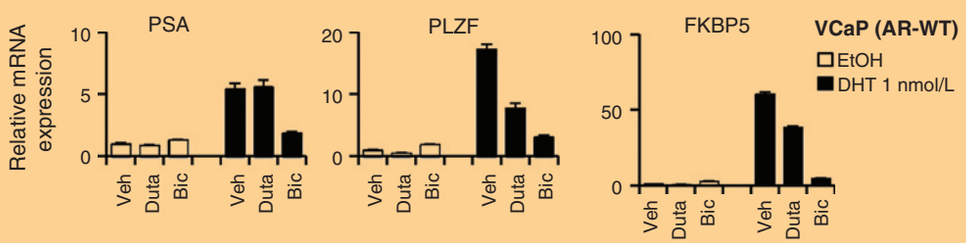
Selected Articles from This Issue

Abiraterone Driven AR Mutations

Chen *et al.* Page 1273

Inhibitors of the enzyme CYP17A1 such as abiraterone are initially effective in men with castration-resistant prostate cancer because they markedly decrease androgen synthesis, but upstream substrates, including progesterone, are increased. Chen and colleagues sequenced the androgen receptor (AR) in a series of tumor biopsies from men who developed resistance to CYP17A1 inhibitors and identified the T878A mutation, which confers responsiveness to alternative ligands, including progesterone, in 4 of 19 cases. These findings indicate that at least a subset of abiraterone-resistant tumors remain AR driven and identifies mutations that can exploit alternative ligands as a mechanism of resistance to abiraterone.



Potential Role of pNF-H as a Predictive Marker of Chemobrain

Natori *et al.* Page 1348

Chemotherapy-induced cognitive impairment (CICI) has been recognized as a clinically significant problem in patients undergoing chemotherapy; however, little is known about the mechanisms and diagnostic measures of CICI. The phosphorylated form of the high-molecular-weight neurofilament heavy subunit NF-H (pNF-H), one of the major structural proteins in axon, has potential as an effective biomarker of neuronal damage. In this study, Natori and colleagues assessed serum pNF-H level in breast cancer patients treated with chemotherapy and found that it was increased in a cumulative dose-dependent manner, suggesting the potential application of pNF-H as a biomarker of neural damage after chemotherapy.

Safety and Efficacy of Oncolytic Adenovirus VCN-01

Rodríguez-García *et al.* Page 1406

Oncolytic viruses infect tumors cells while sparing normal tissues; however, efficacy of virotherapy in the clinic has been hindered by poor tumor targeting and intratumoral dissemination of oncolytic viruses. To tackle simultaneously these drawbacks, the authors present an oncolytic adenovirus, VCN-01, which combines a retargeting modification of the capsid with expression of the extracellular matrix-degrading enzyme hyaluronidase. The pRB-based replication selectivity of VCN-01 allows for a wide applicability in different tumor types. The reported favorable efficacy-toxicity preclinical profile supported two ongoing clinical trials of VCN-01, by intratumoral or intravenous administration, for the treatment of pancreatic cancer and other cancer types.

Integrating RAS Status and Transcriptomic Data in NSCLC

Starmans *et al.* Page 1477

K-Ras is the mostly widely dysregulated oncogene in non–small cell lung cancers, somatically point-mutated in ~30% of adenocarcinomas. To assess the effect of Ras mutation status on prognostic markers for lung cancer, Starmans and colleagues designed targeted and permutation studies and compared biomarker accuracy in RAS-wildtype and RAS-mutant tumours. They find that RAS-mutant tumors are generally more difficult to prognose. Rather than creating a single prognostic biomarker, it is more effective to stratify patients by Ras-status and subject each group to an independent biomarker. These studies provide a template for integrated DNA and RNA biomarkers, as well as providing a new strategy for more accurately personalizing therapy in lung cancer.

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