Clinical Cancer Research

Highlights

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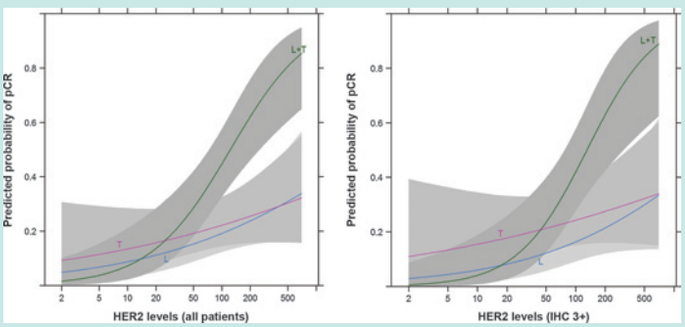
Selected Articles from This Issue



HER2 Expression and Benefit from Dual HER2 Blockade

Scaltriti *et al.* Page 569

It is becoming evident that, among HER2-positive breast tumors, the expression of HER2 is variable. Scaltriti and colleagues investigated the correlation between levels of both HER2 and the truncated isoform p95HER2 in the primary tumors and likelihood to achieve clinical response by anti-HER2 therapy. The authors found that p95HER2 and HER2 expression correlated and that high levels of these receptors predicted for complete tumor remission (and progression-free survival) in response to the combination of trastuzumab and lapatinib. This study proposes HER2 quantification as a tool to identify those patients that are more likely to benefit from dual HER2 therapy.

Efficacy and Exploratory Biomarkers of Dacomitinib in SCCHN

Kim *et al.* Page 544

Predictive biomarkers to epidermal growth factor receptor (EGFR) inhibitors in recurrent and/or metastatic squamous cell carcinoma of head and neck (R/M-SCCHN) have been elusive. Kim and colleagues conducted a phase II biomarker trial of dacomitinib, an oral irreversible pan-HER tyrosine kinase inhibitor, in R/M-SCCHN using next-generation sequencing and digital count technology. Dacomitinib showed significantly higher antitumor activity in R/M-SCCHN patients without PI3K-pathway alteration or inflammatory cytokine expression. Screening for phosphoinositide 3-kinase (PI3K)-pathway alteration and/or inflammatory gene expression could help identify subgroups most likely benefit from dacomitinib in R/M-SCCHN.

A Five-Gene Hedgehog Signature in Medulloblastoma

Shou *et al.* Page 585

Medulloblastoma, a common malignant brain tumor in pediatric and adult patients, has recently been redefined by the molecular pathways that drive tumorgenesis. Sonic hedgehog (SHH) activation has been recognized as a common pathway mutated in these tumors. Shou and colleagues describe the development of a five-gene assay that preselects patients with SHH activated medulloblastoma. Validation of this signature was confirmed in independent data sets with 100% concordance using gene expression profiling. Sonidegib, a SHH inhibitor that targets the upstream mutation in this pathway, including hedgehog, patch and smoothen, which account for approximately 70% of the mutations in this pathway, was evaluated in a prospective clinical trial in adult and pediatric medulloblastoma patients. The five-gene assay accurately predicted 6 of 9 responses and 41/41 nonresponders. This test accurately preselects patients that may respond to this targeted therapy, while allowing those without the target to avoid therapy that would not provide any benefit.

Early Detection of Pancreatic Cancer

O'Brien *et al.* Page 622

O'Brien and colleagues have analysed serum markers CA19-9, CA125, CEACAM1, and REG3A in samples taken years in advance of the clinical presentation of pancreatic cancer. CA19-9 and CA125 were elevated many months prior to diagnosis and in combination improved the performance of CA19-9 alone, with lead times of 20-23 months for test-positive cases. CEACAM1 and REG3A were late markers adding little in combined models. This work challenges the prevailing view that CA19-9 is upregulated late in the course of pancreatic cancer development and suggests its potential for screening high-risk groups, particularly if used longitudinally.

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