Clinical Cancer Research

Highlights

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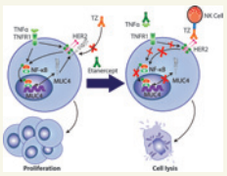
Selected Articles from This Issue

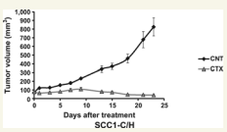
TNFα Induces Trastuzumab Resistance



The monoclonal antibody trastuzumab is the therapy of choice for HER2-positive breast cancer patients, although about 30–45% progress with treatment. Mercogliano and colleagues report a new mechanism of resistance in which the proinflammatory cytokine TNFα induces the expression of mucin 4 (MUC4), which impairs trastuzumab binding and its therapeutic action. The authors show that MUC4 is an independent biomarker of poor disease-free survival in patients treated with adjuvant trastuzumab. These findings postulate MUC4 as a predictive biomarker of response to trastuzumab and provide proof-of-principle to combine this therapy with anti-TNFα drugs to overcome trastuzumab resistance. ■

See article by Mercogliano et al., p. 636

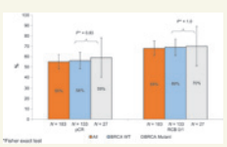
HER3 Targeting Sensitizes HNSCC to Cetuximab



Clinical benefit of anti-EGFR therapy using cetuximab in HNSCC is limited by *de novo* or acquired resistance. To define the role of HER3 in cetuximab resistance and the antitumor mechanisms of EGFR/HER3 dual targeting in HNSCC, a cetuximab-resistant cell line and patient-derived xenograft models (PDX) were analyzed. Wang and colleagues demonstrate that cetuximab induces HER3 activation and HER2/HER3 dimerization. HER3 knockdown reduces HER2 activation and resensitized cells to cetuximab. EGFR and HER3 dual targeting was superior to EGFR targeting alone in both the cell line and in PDX. These results support multiple targeting strategies in patients who have failed cetuximab-based therapy. ■

See article by Wang et al., p. 677

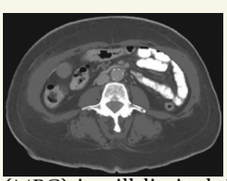
Neoadjuvant Platinum-Taxane Combination Chemotherapy in TNBC



Pathologic and molecular similarities between sporadic and germline *BRCA* mutation associated triple-negative breast cancers (TNBC) have led to the exploration of DNA-damaging agents like platinum compounds in TNBC. Sharma and colleagues report robust pathologic complete-response rates in 190 patients treated with anthracycline-free chemotherapy regimen of carboplatin plus docetaxel. Germline *BRCA*1/2 mutations may be an important biomarker of response to platinum agents in TNBC. It has been speculated that improvement in pCR with addition of carboplatin to traditional chemotherapy in TNBC may be driven primarily by high responses in germline BRCA mutation carriers. The platinum-taxane chemotherapy regimen evaluated in this study, however, rendered equally high pathologic-complete response rates in *BRCA*-associated (pCR of 59%) and *BRCA*-wildtype (pCR of 56%) TNBC. The results of this study support further evaluation of anthracycline-free, platinum-taxane chemotherapy in both *BRCA*-associated and wild-type TNBC. ■

See article by Sharma et al., p. 649

Skeletal Muscle and Outcomes in Metastatic Breast Cancer



Novel concepts regarding the relationship between skeletal muscle measures and chemotherapy toxicity are emerging; however, data regarding this relationship in metastatic breast cancer (MBC) is still limited. In a sample of patients with MBC receiving taxane-based chemotherapy, Shachar and colleagues analyzed different skeletal muscle measurements to show that patients identified as having poorer muscle measures have more treatment-related adverse outcomes such as grade 3-4 CTCAE toxicities, hospitalizations, and other adverse events. This study shows that muscle measurements obtained from computed tomography images performed during routine oncologic care have the potential to individualize chemotherapy dosing better than body surface area. ■

See article by Shachar et al., p. 658