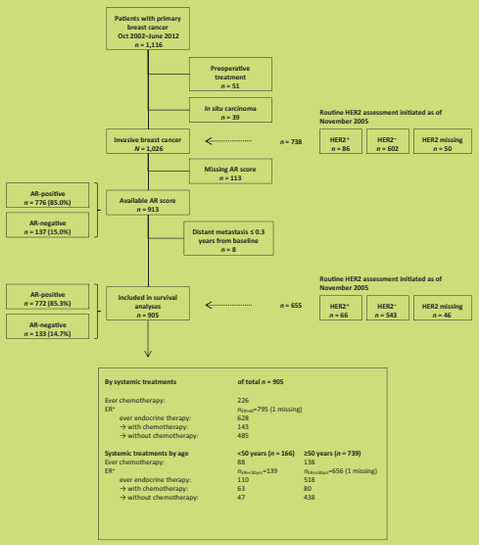
Clinical Cancer Research

Highlights

August 15, 2015 • Volume 21 • Number 16

Selected Articles from This Issue



Androgen and Estrogen Receptor Status in Breast Cancer

Elebro *et al.* Page 3640

In this prospective, population-based epidemiological cohort study of 1,026 patients with primary invasive breast cancer, a significantly differential prognostic role of the androgen receptor (AR) tumor expression in patients with estrogen receptor alpha (ER)-positive and ER-negative tumors was demonstrated. Furthermore, AR-negativity was predictive of early treatment failure to aromatase inhibitors, but not to tamoxifen, among chemonaïve patients aged 50 or older with ER-positive tumors. The results warrant confirmation in an independent study, preferably in a randomized trial. In conclusion, AR tumor assessment may be useful in the clinical setting for improved tailoring of breast cancer treatment.

Antigen Spread after Treatment with Sipuleucel-T

GuhaThakurta *et al.* Page 3619

Antigen spread, an adaptive immune response to nontargeted tumor antigens following treatment with an antigen-specific immunotherapy may indicate tumor cell destruction and subsequent recognition of additional antigens. Using samples from a phase 3 clinical trial, GuhaThakurta and colleagues showed that antigen spread occurs within weeks of administration of sipuleucel-T, a cellular immunotherapy for prostate cancer directed against prostatic acid phosphatase. Most significantly, antigen spread was found to correlate with overall survival. These results suggest that antigen spread may serve as a posttreatment biomarker for the efficacy of immunotherapy, a finding with broad implications for the field of tumor immunology.

High-Dose Radiation Transforms Tumor Microenvironment

Filatenkov *et al.* Page 3727

Filatenkov and colleagues found that the high-dose radiation transformed the immunosuppressive tumor microenvironment by inducing an intense $CD8^+$ T cell tumor infiltrate, and a loss of myeloid derived suppressor cells (MDSCs). The change was dependent on antigen cross-presenting $CD8^+$ dendritic cells, secretion of IFN-γ, and $CD4^+$T cells expressing CD40L. Antitumor $CD8^+$ T cells entered tumors shortly after radiotherapy, reversed MDSC infiltration, and mediated durable remissions in an IFN-γ dependent manner. Interestingly, extended fractionated radiation regimen did not result in robust $CD8^+$ T-cell infiltration.

Targeting STAT3 in MDSCs from Prostate Cancer Patients

Hossain *et al.* Page 3771

Prostate cancers develop immunosuppressive microenvironment resisting current treatments and the emerging immunotherapies. Hossain and colleagues identified a population of $Lin^-CD15^{HI}CD33^{LO}$ granulocytic MDSCs (G-MDSCs) accumulating in patients during prostate cancer progression. The G-MDSCs secreted large amounts of Arginase 1, thereby suppressing T cells' proliferation and activity. The MDSC functions were under control of the STAT3 transcription factor and a central immune checkpoint regulator. To functionally eliminate prostate cancer-associated G-MDSC, the authors successfully employed an siRNA-based approach to silence *STAT3* specifically in TLR9-expressing G-MDSCs. These findings underscore the potential of oligonucleotide-based therapeutics to alleviate immunosuppressive signaling in advanced prostate cancers.