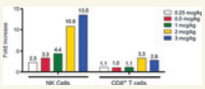
Clinical Cancer Research
Highlights
April 1, 2018 • Volume 24 • Number 7

Selected Articles from This Issue

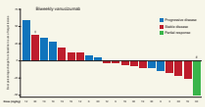
Phase 1 Trial of Subcutaneous rhIL15 in Advanced Solid Tumors



Preclinical experiments demonstrate that interleukin-15 (IL-15) can control homeostasis and stimulate natural killer (NK) and antigen-specific $CD8^+$ T cell activity without causing activation induced cell death or promoting T regulatory (Treg) cell function. Miller and colleagues conducted the first-in-human outpatient phase I dose escalation of subcutaneous (SC) rhIL-15 in refractory solid tumor cancer patients. SC rhIL-15 treatment was well tolerated and resulted in substantial increases in circulating NK and $CD8^+$ T cells. These results will allow the export of IL-15 immunotherapy to an outpatient setting and testing of combinatorial strategies to improve cancer treatment. ■

See article by Miller et al., p. 1525

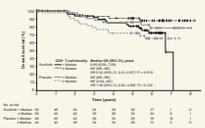
Phase I Study of Vanucizumab



Treatment of cancer by targeting VEGF-A with bevacizumab has been extensively validated in the clinic; however, not all tumors respond to VEGF-A blockade. Angiopoietin-2 (Ang-2) and VEGF-A have complementary roles in regulating tumor angiogenesis and metastasis, suggesting that dual pathway inhibition is necessary to improve treatment outcomes. Vanucizumab is an investigational, first-in-class, bi-specific IgG1-like monoclonal antibody that simultaneously blocks VEGF-A and Ang-2 from interacting with their receptors. Hidalgo and colleagues conducted a first-in-human study that demonstrated an acceptable safety and tolerability profile for vanucizumab in patients with advanced solid tumors. Vanucizumab also demonstrated consistent pharmacokinetic and pharmacodynamic effects, and showed encouraging signs of antitumor activity that support further evaluation of vanucizumab in clinical trials. ■

See article by Hidalgo et al., p. 1536

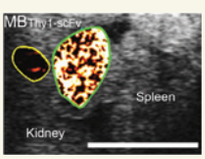
Immune Biomarkers for Adjuvant Sunitinib in Locoregional RCC



Adjuvant sunitinib prolonged disease-free survival over placebo in patients with locoregional renal cell carcinoma at high risk of recurrence postnephrectomy in the randomized phase III STRAC trial. In a prospectively designed exploratory analysis of tissue samples from a subset of patients in this trial, George and colleagues identify predictive biomarkers that could facilitate future patient selection for adjuvant sunitinib and mechanisms of interaction that might explain the durable treatment effect, potentially leading to future combination approaches. Tumor tissue expression levels of CD4, CD8, CD68, and PD-L1 were compared with efficacy outcomes. The observed association between higher $CD8^+$ T-cell density in tumor tissue with longer disease-free survival with sunitinib, but not placebo, suggested predictive potential of $CD8^+$ T-cell density, which warrants further independent cohort validation studies. The prognostic value of PD-L1 expression in primary tumors in this setting also should be further explored. ■

See article by George et al., p. 1554

PDAC Imaging using Thy1-Targeted Ultrasound Contrast Agent



The thymocyte differentiation antigen-1 (Thy1) is differentially expressed on the neovasculature of human PDAC compared to chronic pancreatitis and normal pancreas. To engineer a human Thy1-binding single-chain-antibody-ligand (Thy1-scFv) conjugated to microbubbles ($MB_{Thy1\text{-}scFv}$), Abou-Elkacem and colleagues designed and validated a clinically translatable Thy1-scFv for contrast-enhanced ultrasound molecular imaging of PDAC. The $MB_{Thy1\text{-}scFv}$ was highly specific to murine/human Thy1, and *in vivo* ultrasound molecular imaging of PDAC-bearing mice demonstrated specific binding to Thy1. Ongoing translational studies are targeted at developing clinical-grade $MB_{Thy1\text{-}scFv}$ which may improve visualization of PDAC and enable diagnosing at earlier disease state to ultimately improve survival of PDAC patients. ■

See article by Abou-Elkacem et al., p. 1574

Clinical Cancer Research

Highlights of This Issue

Clin Cancer Res 2018;24:1511.