Clinical Cancer Research

Highlights

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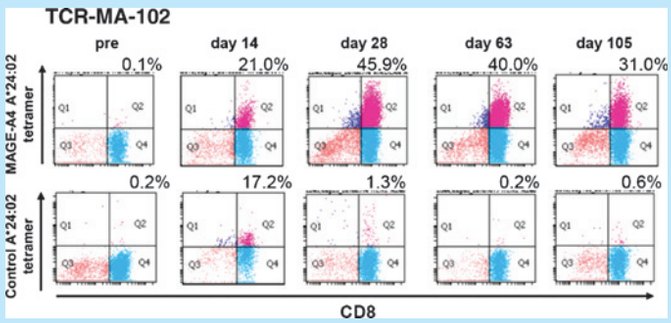
Selected Articles from This Issue



MAGE-A4 TCR Transduced T-cell Transfer for Esophageal Cancer

Kageyama *et al.* Page 2268

TCR-gene T-cell therapy has been studied in refractory melanoma and sarcoma patients, and the regimens usually include lymphodepleting preconditioning. Kageyama and colleagues treated 10 MAGE-A4+ recurrent esophageal cancer patients with wild-type TCR-gene transduced T-cell transfer. They show that the transferred T cells persisted long, trafficked to tumor sites, and maintained tumor-specific reactivity and that 3 of 10 patients who had minimal disease long-remained free from disease progression. All the patients did not encounter any serious toxicity. Wild-type TCRs with physiologically high avidity may represent a safe approach in clinical use.

Clinical and Preclinical Assessment of JNJ-38877605

Lolkema *et al.* Page 2297

The development of novel anticancer agents is central to improving cancer treatment. Lolkema and colleagues present a study exploring a novel selective C-Met inhibitor and report unexpected renal toxicity in humans. Extensive preclinical analysis showed that species-specific metabolism of quinoline ring structures causes the renal toxicity. This integrated clinical and preclinical analysis elucidated the mechanism of toxicity allowing future quinoline ring structure containing drugs to be tested for species specific metabolism.

Intracellular Delivery of GO-203 in Novel Tetrablock Nanoparticles

Hasegawa *et al.* Page 2338

Cell-penetrating peptides represent a promising class of anticancer drugs; however, these agents have had limited applicability because of poor pharmacologic and intracellular delivery properties. Hasegawa and colleagues report that these challenges can be circumvented when targeting the widely overexpressed MUC1-C oncoprotein by encapsulating the GO-203 inhibitor peptide in novel biodegradable PLA-PEG-PPG-PEG tetrablock nanoparticles (NPs). They show that these NPs are highly effective for inhibiting MUC1-C by the sustained intracellular delivery of GO-203 in diverse carcinoma cells growing *in vitro* and *in vivo*. This NP-based approach may be functional for the targeting of other intracellular oncoproteins with peptide drugs.

Crizotinib Resistance in *ROS1*-Rearranged NSCLC

Song *et al.* Page 2379

Crizotinib showed marked antitumor activity against *ROS1*-rearranged NSCLC. Despite the efficacy of crizotinib, development of resistance is inevitable. Song and colleagues discerned the mechanisms of crizotinib resistance in *ROS1*-rearranged NSCLC using samples from two patients and crizotinib-resistant cell lines. *ROS1* kinase mutations (G2032R and L2155S), EGFR activation, and epithelial-to-mesenchymal transition were associated with acquired crizotinib resistance. Secondary *ROS1*-mutant NSCLC cells were sensitive to foretinib. In addition, EGFR/ROS1-activated NSCLC cells were inhibited by irreversible EGFR inhibitors. These might define subsequent treatment strategies in patients with *ROS1*-rearraged NSCLC who showed acquired resistance to crizotinib.

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