Clinical Cancer Research
Highlights
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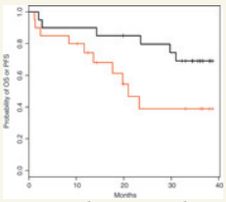
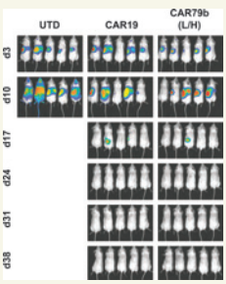
^{177}Lu-Satoreotide Tetraxetan in Well-Differentiated NETs



Peptide receptor targeted radionuclide therapy (PRRT) with the somatostatin receptor (sstr) *agonist* ^{177}Lu-DOTA-TATE has recently been approved for treatment of advanced neuroendocrine tumors (NETs). Preclinical studies have suggested improved targeting of NETs with radiolabeled sstr *antagonists*. This phase I clinical trial of the sstr *antagonist* ^{177}Lu-Satoreotide Tetraxetan showed a promising response rate, but also revealed unexpectedly common and severe hematotoxicity. Hematotoxicity occurred at bone marrow radiation doses considered as safe for ^{177}Lu-DOTA-TATE. These results emphasize the need for careful dose finding studies of new PRRT ligands even if the target and radionuclide are identical. ■

See article by Reidy-Lagunes et al., p. 6939

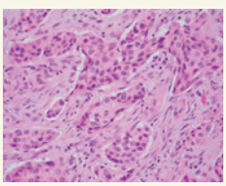
CAR T Cells Targeting CD79b



Anti-CD19 chimeric antigen receptor (CAR) T cells have emerged as a leading therapy for relapsed/refractory B-cell non-Hodgkin lymphomas. However, disease relapses can occur due to antigen escape. To overcome this mechanism of resistance, Ormhøj and colleagues developed a CAR targeting CD79b, an antigen retained on B-cell lymphoma cells independently of CD19 loss. CAR T cells engineered to recognize CD79b alone or in combination with CD19 successfully cleared lymphoma in mouse models even when CD19 expression was heterogeneous or negative. These results show promise for clinical efficiency in B-cell lymphoma patients and may prevent or treat CD19-negative relapse. ■

See article by Ormhøj et al., p. 7046

Broad Panel NGS for NSCLC Clonality Assessment



Patients with >1 non-small cell lung carcinoma (NSCLC) are encountered commonly in current practice. The distinction whether such patients have separate lung primary carcinomas versus intrapulmonary metastases of a single tumor is a clinically-relevant diagnostic dilemma for which the diagnostic approach is evolving. The study by Chang and colleagues documents the utility of comprehensive next-generation sequencing (NGS) for unambiguously establishing clonal relationships among NSCLCs. These findings have the potential to revolutionize the approach to multiple NSCLCs in clinical practice, and they illustrate the utility of comprehensive NGS not only for identification of targetable alterations, but also for assessment of tumor clonal relationships. ■

See article by Chang et al., p. 7113

CAR-NKTs Mediate Long-Term Control of Neuroblastoma in Mice

T cells expressing chimeric antigen receptors (CAR-T) remain largely ineffective against solid tumors in part due to poor localization to and survival at tumor sites. Xu and colleagues exploited the intrinsic tumor-trafficking properties of natural killer T cells and directed them against neuroblastoma *via* expression of GD2-specifc CAR constructs (CAR-NKT) alone or in combination with IL-15. CAR-NKT coexpressing IL-15 demonstrated superior functional fitness, prolonged *in vivo* persistence with tumor infiltration, and long-term tumor control in mice without causing significant toxicity. These results enabled implementation of first-in-human CAR-NKT clinical testing. ■

See article by Xu et al., p. 7126