Clinical Cancer Research **Highlights**

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Selected Articles from This Issue

Preclinical Activity of MLN9708 in Myeloma Bone Disease

Garcia-Gomez *et al.* **Page 1542**

MLN9708 (ixazomib citrate) is an oral next-generation proteasome inhibitor (PI) currently in phase III trials in multiple myeloma patients, but with a yet-unknown effect on myeloma-associated bone disease. Garcia-Gomez and colleagues show that clinically relevant concentrations of ixazomib promote osteoblast differentiation and function and inhibit osteoclast formation and resorption *in vitro*. Also, in a disseminated myeloma mouse model, ixazomib controls myeloma growth and prevents bone loss, as assessed by bone-forming and anticatabolic activities. Thus, it is conceivable that MLN9708, similar to the first-in-class PI bortezomib, will achieve beneficial bone effects, in addition to antimyeloma activity in myeloma patients.

Hedgehog Signaling in Squamous Cell Lung Cancer

Huang *et al.* **Page 1566**

Hedgehog-GLI signaling is upregulated in a proportion of lung squamous cell carcinoma (LSCC), but no studies to date evaluate its role in LSCC. Here, Huang and colleagues identified overexpression of HEDGEHOG-GLI components in the classical subtype of LSCC *via* genomic analysis. In representative cell lines, they demonstrated that GLI2 was important for LSCC cell survival, whereas SMOOTHENED plays a minor role. Importantly, they reported that the GLI inhibitor GANT61 successfully suppressed tumor growth both *in vitro* and *in vivo* and thus shows promise as a novel targeted therapy for a subset of LSCC patients.

Radiographic Response to Therapy Predicts Survival

Liu *et al.* **Page 1623**

The combination therapy of sorafenib and TACE is considered an alternative for patients with unresectable HCC. The assessment of tumor response to this therapy is particularly crucial in determining treatment success. To define the earliest time at which the response to combination therapy could be accurately assessed, Liu and colleagues demonstrated that the available criteria EASL and mRECIST responses assessed after 3 to 4 months of therapy are more reliable for detecting the early changes in the tumor and can be considered valuable early indicators for making subsequent therapeutic decisions and predicting long-term survival.

Noninvasive Quantitative Genotyping of Cell-Free Plasma DNA

Oxnard *et al.* **Page 1698**

Analysis of cell-free plasma DNA represents an attractive strategy for noninvasive genotyping of advanced cancer patients. Oxnard and colleagues designed quantitative plasma-based genotyping assays for *EGFR*, *KRAS*, and *BRAF* mutations using droplet digital PCR and demonstrated a high positive predictive value in patients with advanced lung cancer and melanoma. Serial analysis of plasma from lung cancer patients on a prospective trial of first-line erlotinib demonstrated high pretreatment *EGFR* levels, complete plasma response, and detection of a T790M resistance mutation weeks prior to clinical progression, suggesting potential as a noninvasive clinical tool for characterizing treatment response and resistance.

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