Clinical Cancer Research

Highlights

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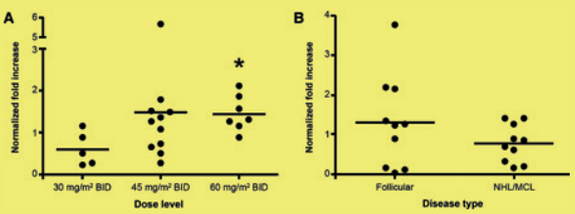
Selected Articles from This Issue



Abexinostat in Mantle Cell and Follicular Lymphoma

Evens *et al.* Page 1059

Evens, et al, investigated the use of abexinostat, an oral pan-histone deacetylase inhibitor in patients with relapsed/refractory lymphoma. Abexinostat was particularly efficacious in follicular lymphoma with a 64% response rate in evaluable patients. Furthermore, responses were durable with median duration of response not reached and median progression-free survival of 20.5 months. Using unique intermittent dosing, abexinostat was well tolerated with thrombocytopenia, fatigue, and neutropenia as the only grade 3/4 adverse events occurring in ≥10% of patients. Altogether, abexinostat represents a potential new treatment for lymphoma and further investigation is warranted.

T790M by Tumor Biopsy versus Blood-Based Analyses

Sundaresan *et al.* Page 1103

Sundaresan and colleagues evaluated T790M genotypes in 40 patients with progressing EGFR-mutant lung cancer, comparing concurrently obtained tumor biopsies, circulating tumor cells (CTCs), and circulating tumor DNA (ctDNA). Concordance between the blood-based methods and tissue biopsy was approximately 70%, and when used in combination, the two blood-based methods enabled successful genotyping in all patients. Blood-based genotyping also identified the T790M mutation in 35% of patients in whom the concurrent tumor biopsy was negative or nondiagnostic. Discrepant genotyping results between biopsy, CTCs, and ctDNA likely reflect both technical variation as well as biological differences in the tumor material sampled by these assays. Without a reliable "gold standard," the clinical utility of different T790M-genotyping strategies will ultimately be determined by their ability to predict clinical responses to novel EGFR inhibitors.

Targeting of BCL2 Proteins in Diffuse Large B-cell Lymphoma

Klanova *et al.* Page 1138

Defects in apoptotic signaling, including overexpression of BCL2 antiapoptotic proteins, contribute to increased survival of diffuse large B-cell lymphoma (DLBCL) cells and might result in resistance to conventional genotoxic agents. By targeting BCL2 and MCL1 proteins, Klanova and colleagues demonstrated that DLBCL can be divided into BCL2- and MCL1-dependent subgroups. In addition, the authors showed that concurrent inhibition of BCL2 and MCL1 was highly synergistic *in vitro* and *in vivo* using primary cell-based murine xenograft models of DLBCL. These findings might have implications for concepts of early clinical trials in DLBCL.

PRAME as a Biomarker in Uveal Melanoma

Field *et al.* Page 1234

Primary uveal melanomas are conventionally divided into Class 1 tumors (low metastatic risk) and Class 2 tumors (high metastatic risk) based on a prospectively validated gene expression classifier. In this study, a new subgroup of Class 1 uveal melanomas with intermediate metastatic risk is identified based on expression of the immunogenic oncoprotein PRAME. This discovery further optimizes the prognostic accuracy of the gene expression classifier and identifies patients who may be good candidates for immunotherapy.

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