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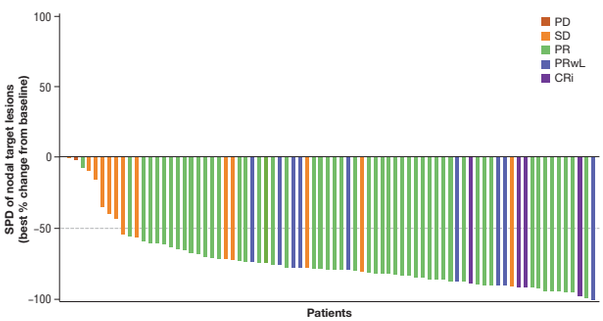
CLINICAL CANCER RESEARCH

HIGHLIGHTS

Selected Articles from This Issue

DUO Duvelisib Crossover Extension Study



Davids *et al.* | Page 2096

Patients with relapsed/refractory (R/R) CLL/SLL have an urgent need for effective and tolerable treatments. To this end, Davids and colleagues evaluated the efficacy and safety of duvelisib, an oral PI3K-δ,γ inhibitor, in patients with CLL/SLL in a crossover extension study following disease progression on ofatumumab during the DUO trial. Duvelisib demonstrated high response rates, good durability, and a manageable safety profile in these patients, including those with high-risk disease and ofatumumab-refractory disease. These results provide additional evidence for duvelisib as an effective treatment option for difficult-to-treat patients with R/R CLL/SLL and support the development of further prospective studies of this agent.

Bone Metabolic Markers to Monitor Radium Therapy in mCRPC

Agarwal *et al.* | Page 2104

Bony metastases occur in most patients with metastatic castration-resistant prostate cancer (mCRPC) and are associated with significant morbidity. Radium-223, a calcium mimetic that accumulates in bones and emits alpha radiation, improves survival outcomes in mCRPC. However, monitoring the response to radium223 is not currently feasible, necessitating surrogate markers of treatment outcomes. To assess the utility of bone metabolic markers (BMM) in this capacity, Agarwal and colleagues conducted a prospective phase II trial of radium-223 plus enzalutamide versus enzalutamide alone in patients with mCRPC. Assessment of BMMs revealed that radium-223 was associated with decrease in serum BMM and improved outcomes. These data may allow BMM to be used for assessing response to therapy in future trials of novel radioisotopes for bony metastases in mCRPC.

Plasma Thymidine Kinase Activity and Palbociclib Treatment

McCartney *et al.* | Page 2131

Thymidine kinase 1 (TK1) is an enzyme critical to synthesis of DNA and cell proliferation. McCartney and colleagues demonstrate that TK1 activity is reduced in palbociclib-sensitive breast cancer cell lines following exposure to palbociclib; this reduction was detected earlier than a corresponding decrease in cell proliferation. Plasma TK1 levels were assessed in women with breast cancer treated with palbociclib as part of a phase II trial. Low plasma TK1 activity was associated with improved prognosis following one cycle of therapy, as well as at the point of disease progression. These results suggest that TK1 can be used as a marker of early resistance to CDK4/6 inhibitors.

Analysis of CSF from LMM Patients

Smalley *et al.* | Page 2163

Leptomeningeal melanoma metastasis (LMM) is a devastating, yet understudied, complication of advanced melanoma. Smalley and colleagues performed proteomic profiling of cerebrospinal fluid (CSF) samples from patients with LMM and detected elevated expression of proteins implicated in innate immunity, tissue damage, and melanoma growth/survival. CSF from patients with LMM also rendered melanoma cells resistant to BRAF inhibition through increased AKT and TGF-β signaling. Further study of the microenvironment of LMM will facilitate the development of targeted therapeutic strategies for this component of advanced melanoma.

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