Clinical Cancer Research
Highlights
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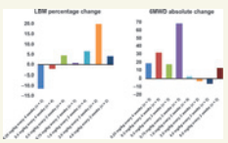
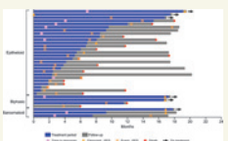
Targeting Cachexia in Advanced Cancer



TGF-beta signaling is involved in many aspects of cancer progression, including cachexia. In a first-in-human phase I trial, Tao and colleagues describe the effects of STM 434, which targets the TGF-beta ligand activin A, in advanced solid cancers. Although STM 434 did not yield direct antitumor benefits, this agent did result in favorable metabolic changes, including increased lean body mass and improved 6-minute walk distance. Therefore, targeting activin A shows promise for the management of cancer cachexia. ■

See article by Tao et al., p. 5458

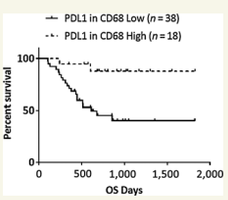
Nivolumab in Japanese Patients with Advanced Malignant Pleural Mesothelioma



Malignant pleural mesothelioma (MPM) is a rare and aggressive malignancy with poor prognosis. In a phase II trial, Okada and colleagues evaluated the efficacy and safety of nivolumab, an immune checkpoint inhibitor, in 34 Japanese patients with advanced or metastatic MPM resistant or intolerant to $\leq$2 chemotherapy regimens. Nivolumab toxicity was manageable, and the objective response rate was 29%, with promising efficacy in all histological subtypes and in patients with PD-L1 $\geq$1% and <1%. These data support the recent National Comprehensive Cancer Network recommendation for nivolumab as second-line treatment of MPM. ■

See article by Okada et al., p. 5485

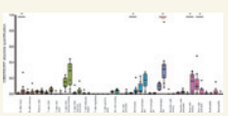
Multiplex Image Analysis Identifies Biomarkers for Melanoma Immunotherapy



Although immunotherapy has provided a benefit to many patients, there is a need to more accurately identify patients who will respond to this treatment. Toward this end, Toki and colleagues utilized a novel multiplex-imaging platform—NanoString GeoMx GSP—that allows for high-plex immune marker quantification. Immune markers were assessed simultaneously in macrophage, leukocyte, and tumor cells. PD-L1 expression in macrophages, specifically, was associated with improved response to immunotherapy. This more specific PD-L1 expression pattern, once translated into the clinic, has the potential to better predict the melanoma patients who will respond well to immunotherapy. ■

See article by Toki et al., p. 5503

Molecular Characterization of Resistance to CRT in Rectal Cancer



Molecular properties associated with response or resistance to chemo/radiotherapy (CRT) are incompletely characterized. Integrated tumor profiling of patient-matched rectal adenocarcinomas before and after neoadjuvant CRT was performed by Kamran and colleagues to identify drivers of radiation resistance and reveal insights into tumor evolution. Unexpectedly, tumor mutational burden and neoantigen load were neither increased after CRT nor associated with treatment response. Poor response was associated with *KRAS/TP53* (KP) co-mutations. Furthermore, nonresponders showed a higher infiltration of M2 macrophages after CRT. These findings highlight the promise of molecular tumor profiling before and after CRT to identify treatment resistance mechanisms and inform novel therapeutic approaches, especially in radioresistant KP tumors. ■

See article by Kamran et al. p. 5561

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