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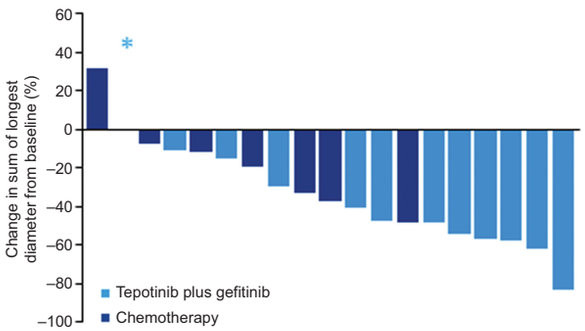
CLINICAL CANCER RESEARCH
HIGHLIGHTS

Selected Articles from This Issue

Tepotinib Plus Gefitinib Versus Chemotherapy in EGFR-Mutant NSCLC



Liam *et al.* | Page 1879

There is a high unmet need for patients with EGFR-mutant non-small cell lung cancer (NSCLC) that have developed resistance to EGFR inhibitors. Liam and colleagues present final analyses from the phase II part of INSIGHT, evaluating tepotinib (a once-daily, highly selective MET inhibitor) plus gefitinib versus chemotherapy in patients with EGFR-mutant NSCLC and MET-driven EGFR inhibitor resistance, with a median follow-up duration of 57.5 months. This long follow-up emphasizes that the greatest benefit from tepotinib plus gefitinib is derived by patients with MET amplification, who showed substantially improved progression-free and overall survival versus chemotherapy in this updated analysis. Furthermore, all patients who received long-term tepotinib plus gefitinib had MET amplification, with 25% of patients with MET amplification receiving combination treatment for >4 years, and 17% for >5 years (including continuing treatment outside the study). Tepotinib plus an EGFR inhibitor is a promising strategy in this disease setting.

ZUMA-7 Analysis: Axi-Cel in Patients ≥65 Years With R/R LBCL

Westin *et al.* | Page 1894

Older patients with relapsed/refractory (R/R) large B-cell lymphoma (LBCL) may be considered ineligible for curative-intent treatments such as high-dose chemotherapy with autologous stem-cell transplantation due to age and/or the presence of comorbidities that increase the risk of intolerable adverse events. In this preplanned subgroup analysis of patients aged ≥65 years enrolled in the ZUMA-7 trial of axi-cel (an autologous anti-CD19 chimeric antigen receptor [CAR] T-cell therapy) versus standard of care (SOC) in second-line R/R LBCL, Westin and colleagues show that CAR T-cell expansion was comparable, with patients aged ≥65 years and axi-cel having significantly improved event-free survival and health-related quality of life over SOC. Although the pharmacodynamic (serum proinflammatory and immune-modulatory analytes, including cytokines and chemokines) profile of axi-cel was elevated post axi-cel infusion in patients ≥65 years versus patients <65 years, adverse events were manageable. Together, these results support axi-cel as a viable and effective curative-intent second-line treatment option for older patients with R/R LBCL.

CTC PSMA Expression and Outcomes in mCRPC

Gupta *et al.* | Page 1929

Gupta and colleagues have developed and validated a liquid biopsy assay for PSMA protein expression in circulating tumor cells, characterizing the heterogeneity of expression in the prospective multicenter PROPHECY clinical trial of men with mCRPC treated with potent AR inhibitors. They identify the independent prognostic significance of PSMA CTC expression on shortened progression-free and overall survival in such patients, and this sets the stage for future predictive studies of the PSMA CTC biomarker in the context of PSMA targeted therapies such as PSMA-Lu177-617 radioligand therapy.

Lactate/PD-1 Inhibition and Activation of Innate Immunity

Chaudagar *et al.* | Page 1952

PTEN loss-of-function (LOF), which hyperactivates the PI3K pathway, occurs in ∼50–75% of metastatic, castrate-resistant prostate cancer (mCRPC) patients and is associated with poor therapeutic outcomes and resistance to immune checkpoint inhibitors. To elucidate the mechanistic basis for limited phase III trial efficacy of dual PI3K/AKT and intensified androgen blockade in patients with PTEN LOF mCRPC, Chaudagar and colleagues utilized a prostate-specific PTEN/p53-deficient genetically engineered mouse model and discovered that cotargeting histone lactylation (with PI3K inhibitor) and PD-1-mediated immunosuppression within TAM, in combination with ADT, drives TAM-mediated phagocytosis and tumor control. Collectively, the findings warrant further investigation in PTEN-deficient mCRPC clinical trials.

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