Clinical Cancer Research

Highlights

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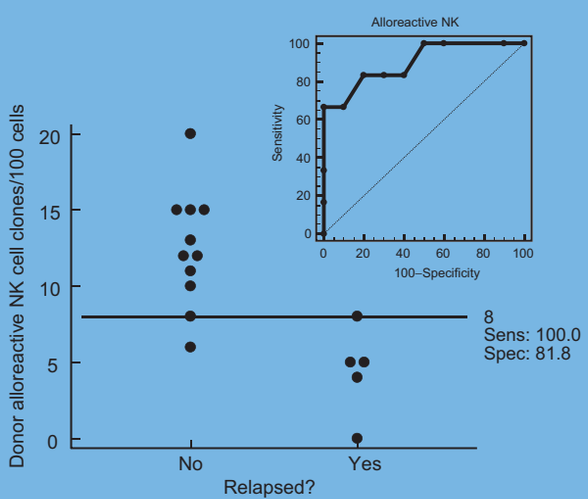
Selected Articles from This Issue



NK Cell Therapy for Elderly AML Patients

Curti *et al.* Page 1914

Curti and colleagues correlated the graft composition with the clinical outcome of 17 elderly patients with AML undergoing NK cell immunotherapy after induction/consolidation. AML patients received NK cells from haploidentical KIR-ligand mismatched donors after immunosuppression, followed by interleukin-2. The authors demonstrated that larger size of donor alloreactive NK cell repertoire correlates with better response to immunotherapy. Such finding represents a proof-of-concept of the antileukemic role of NK alloreactivity and has implications for the choice of the most suitable donor.

Stat3/5 Signaling Architecture in High-Risk MDS

Miltiades *et al.* Page 1958

Molecular predictors of response and mechanisms of resistance to azacytidine in Myelodysplastic syndrome (MDS) remain largely unidentified. Abnormal Stat3/5 signaling is implicated in clonal hematopoiesis. To explore the Stat3/5 signaling architecture in MDS, Miltiades and colleagues performed functional phenotyping in MDS patients undergoing azacytidine treatment. The Stat3/5 signaling biosignature identified patients in poor prognosis and marked a pathophysiologically and prognostically relevant, azacytidine resistant, $CD34^+$ subset, whose kinetics paralleled the disease course and response to azacytidine. Their findings suggest that the aberrant Stat3/5 biosignature in MDS may represent a response predictor and also a therapeutic target to overcome azacytidine resistance.

Cytotoxicity of Ixazomib for $NPMc^+$ AML

Garcia *et al.* Page 1978

A mutation in *NPM1* is one of the most common recurring genetic lesions in AML. To explore its role in rendering acute leukemia cells susceptible to ixazomib, a recently approved second-generation proteasome inhibitor for multiple myeloma, Garcia and colleagues evaluated the oxidative stress response in mediating cytotoxic activity. A direct association was observed between $NPMc^+$ expression in AML, reduced antioxidant responses, and enhanced sensitivity to an oral proteasome inhibitor that induces oxidative stress. These data suggest that intracellular determinants of antioxidant responses may be good predictors of therapeutic response to ixazomib.

Intraclonal Diversification of IG Genes in SMZL

Bikos *et al.* Page 2032

The high frequency of the IGHV1-2*04 immunoglobulin gene in splenic marginal zone lymphoma (SMZL) strongly indicates antigen selection in disease development. IGHV1-2*04 expressing cases account for one-third of all SMZL and constitute a disease subgroup with a distinctive profile of genomic aberrations and an overall worse prognosis, indicating that immune signaling mediated by distinctive immunoglobulin receptors may impact on SMZL clonal behavior and eventual patient outcome. The present study advances the understanding of SMZL pathogenesis showing that ongoing antigen involvement is relevant throughout the natural history of SMZL, particularly IGHV1-2*04 cases, thus offering a strong rationale for signaling inhibition therapy.

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