From the Editor

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The September issue of the *American Journal of Hematology/Oncology* continues the trend in immunotherapy, this time, extending to lung and breast cancer. Most oncologists are not yet using much immunotherapy, as the new checkpoint inhibitors are only approved in melanoma, and more recently in lung cancer. But renal cell, liver, and several other cancers will most likely follow.

This issue takes you into the future of lung and breast cancer immunotherapy. What are we learning, and what are the highest-impact opportunities? Dr Goldberg summarizes the rapidly growing body of evidence for checkpoint inhibitors (pembrolizumab and nivolumab) in non-small cell lung cancer, while Drs Mittendorf and Hunt discuss the broad array of immunological levers, including checkpoint inhibitors and active vaccine therapy, being tested in breast cancer.

Many questions need to be addressed beyond demonstrating activity. The priorities for clinical trials have been historical success (eg, melanoma) as well as some demonstration of innate immunity, usually manifest as lymphocytic infiltration in the tumor and surrounding stroma. For example, in breast cancer, there has long been an appreciation that in the triple-negative subset (in particular, "medullary carcinoma," which is a common subtype in *BRCA* mutation carriers), such infiltrates are more common and predict a better long-term outcome with standard chemotherapy. We now know that this subtype of breast cancer has more mutations, and presumably more "neoepitopes" to activate the immune system. In HER2+ breast cancer, there is evidence that an immune reaction may be as effective as adjuvant trastuzumab, which itself probably works as much as an immune modulator (by activating antibody-dependent cellular cytotoxicity) as it does via HER2 receptor signaling pathway inhibition.

Still, the metrics that predict success of immunotherapy are far from established. Expression of the PD-L1 ligand, as well as the immunophenotype of the lymphocytic infiltrate, are being studied as predictive factors. Also, strategic combinations of checkpoint inhibitors, vaccines, granulocyte-macrophage colony-stimulating factor, immunostimulatory agents (eg, toll-like and OX40 receptor agonists), and even growth factor receptor pathway modulators are showing promise in early-phase studies. One emerging difference of immune therapy appears to be its lasting effect, with longer remissions possible as tumor cells find it hard to evade the immune onslaught, in contrast to "bypass" pathways that emerge within growth-signaling networks in response to growth factor–targeting drugs. It is hoped that demonstration of success in advanced disease will lead to even greater gains in the adjuvant setting—especially if toxicity is manageable. These trials are already designed and will be activated soon. We will certainly be revisiting this area regularly in future issues of the Journal.