Clinical Pathology Selected Abstracts, 3/15

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Chimeric antigen receptor T cells for sustained remissions in leukemia

Defining and managing incidental findings in genetic and genomic practice

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Chimeric antigen receptor T cells for sustained remissions in leukemia

Relapsed and refractory acute lymphoblastic leukemia is associated with a poor prognosis. T cells genetically modified to express chimeric antigen receptors targeted to cells expressing CD19 (CTL019) are a promising treatment strategy, with complete responses previously reported in two patients who had relapsed and refractory acute lymphoblastic leukemia (ALL). The authors conducted a study to assess the outcomes, persistence of CTL019 cells, and adverse effects in an expanded cohort with relapsed and refractory ALL who were treated with CTL019 cell infusions. They enrolled in the study 30 patients (25 pediatric and five adult) with relapsed and refractory ALL who then received CTL019 cell infusions. One month after infusion, 27 (90 percent) patients achieved complete morphologic remission. Twenty-two patients at one-month post-infusion and 24 patients at three months post-infusion had no detectable minimal residual disease. Two patients with central nervous system (CNS) disease at the time of infusion had no detectable CNS disease six months later. Of the 27 patients who initially achieved complete remission, seven relapsed. Relapses were attributed to early loss of CTL019 cells (three patients), loss of CD19 expression on leukemic cells (three patients), and persistence of disease (one patient). Six months after infusion, the event-free survival rate was 67 percent, and the overall survival rate was 78 percent. The probability of CTL019 cell persistence in peripheral blood six months after infusion was 68 percent. The probability of relapse-free B cell aplasia, which was used as a measure of CTL019 function, was 73 percent six months after CTL019 infusion. The study concluded that CTL019 cell therapy is a promising strategy to treat relapsed and refractory ALL, with high short-term response rates and prolonged persistence of infused cells.

Maude SL, Frey N, Shaw PA, et al. Chimeric antigen receptor T cells for sustained remissions in leukemia. *N Engl J Med.* 2014;371:1507–1517.

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Defining and managing incidental findings in genetic and genomic practice

Decreasing costs for genomic testing have resulted in a shift from targeted sequencing approaches to sequencing of the entire exome or genome. The greater the resolution by which the genome is analyzed, the greater the likelihood of finding potential genetic abnormalities that are unrelated to the initial diagnosis or clinical questions. These incidental findings (IFs), a term used in radiology and biochemistry, are now a topic of interest for clinicians, researchers, and commercial providers of genetic testing. Many argue that the patient should be made aware of the potential for IFs. In this study, the authors reviewed recent literature about IFs, including terminology, types of information to be communicated, and implications for clinical management. They searched databases, including PubMed, Embase, and Google Scholar, to identify terms that would be synonyms for incidental finding. Other

searches included websites and relevant journals. The authors discovered a lack of standard terminology used for IFs and situations in which IF may not be the best term, as well as uncertainties about determining clinical utility and when to disclose incidental findings. They noted that, just like in the field of medical imaging, the management and communication of IFs needs international consensus and not just ad hoc approaches. However, their literature review suggests that there is widespread agreement that clearly pathogenic IFs identified in clinical practice, when treatment of care is available or may become available, should be communicated. The authors recommend that consent for disclosure of IFs be sought whenever possible. Yet how best to do this needs to be worked out and evaluated. In very complex situations, in which genome sequencing is providing patients with unanticipated results, the authors concluded that viewing genome output as a resource, accessible over time, may be the best approach. In this way, clinicians may disclose information appropriately and recontact patients when the significance of a previous IF is known.

Shkedi-Rafid S, Dheensa S, Crawford G, et al. Defining and managing incidental findings in genetic and genomic practice. *J Med Genet.* 2014;51:715–723.

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