Toxicity Management

Development of a novel and immune-mediated adverse events algorithm

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BACKGROUND: Novel immunotherapy and biologic agents are being developed with the potential to improve outcomes and reduce long-term toxicities among individuals with hematologic malignancies. These emerging drugs affect neoplastic cells and the surrounding microenvironment, causing unique immune-mediated toxicities.

OBJECTIVES: The aim was to develop an algorithm for clinical staff to manage unique toxicities associated with next-generation immunotherapies indicated in the hematologic population, using a system-focused approach.

METHODS: Data were collected using specific toxicities based on the four major novel biologic classes. Immune-mediated adverse events were reported across studies. Based on published literature, institutional experience, and group consensus, a novel algorithm for managing immune-mediated toxicities was created.

FINDINGS: The development of this treatment algorithm provides a more streamlined approach for managing common but unique toxicities and improves safety, compliance, patient outcome, and quality of life with novel immuno-oncologic agents.

KEYWORDS
immunotherapy; toxicities; novel agents; immune-mediated; adverse events

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TWO MAJOR LYMPHOMA CATEGORIES EXIST, Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). These two categories comprise a group of lymphoproliferative diseases with an incidence of 55,000–60,000 new cases each year (Alinari, Quinion, & Blum, 2015). The foundation of treatment for B-cell lymphomas consists of traditional chemotherapy agents, including alkylating agents, anthracyclines, purine analogs, and monoclonal antibodies. To date, the mainstays of treating NHL are dependent on the specific subtype of lymphoma. Indolent lymphomas, such as follicular lymphoma (FL), marginal zone lymphoma (MZL), and small lymphocytic lymphoma (SLL), may be managed using an observation-only approach (Horning & Rosenberg, 1984; Yuda et al., 2016), a single-agent monoclonal antibody (Weiner, 2010), or a combined chemotherapeutic approach (Rummel et al., 2013). In comparison, more aggressive lymphomas are almost always treated with traditional chemotherapy regimens, such as rituximab (Rituxan®), cyclophosphamide (Cytoxan®), doxorubicin (Adriamycin®), vincristine (Oncovin®), and prednisone (Deltasone®), also known as R-CHOP (Feugier et al., 2005; Peyrade et al., 2017). HL is generally treated with doxorubicin, bleomycin (Blenoxane®), vinblastine (Alkaban®), and dexamethasone (Decadron®), also known as ABVD (Diefenbach et al., 2016; Meyer et al., 2005). Traditional chemotherapeutic approaches are associated with nonspecific toxicity, including myelosuppression, mucositis, alopecia, fatigue, nausea, and vomiting, which are related to the drug’s cytotoxic effect on normal cells (Bhatt, Alejandro, Michael, & Ganetsky, 2014).

Novel biologic agents are being developed with the potential to improve outcomes and reduce long-term toxicities. New cellular targets have been identified, leading to the development and introduction of specific nonchemotherapeutic regimens. These targets include regulators of the cell cycle and specific surface antigens (Alinari et al., 2015). Targeted therapy has the potential to increase efficacy related to its highly specific nature. In addition, this direct activity allows for fewer cytotoxic effects on normal cells compared with traditional chemotherapeutic agents (Bhatt et al., 2014).

Four major novel biologic classes are in development or have recently received U.S. Food and Drug Administration (FDA) approval for patients with hematologic malignancies, and specifically those with B-cell lymphomas: immunomodulatory drugs (IMiDs), programmed death-ligand 1