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Interprofessional Collaboration with Immune Checkpoint Inhibitor Therapy: the Roles of Gastroenterology, Endocrinology and Neurology

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Objectives: *To discuss immune checkpoint inhibitor therapy and identify opportunities for interprofessional collaboration in the management of toxicities in the areas of gastroenterology, endocrinology, and neurology.*

Data Sources: *Published research and education articles in oncology, nursing, and various specialties.*

Conclusion: *The use of immune checkpoint inhibitors is expanding; timely management of toxicity is critical for positive patient outcomes. There are many opportunities for interprofessional collaboration in the diagnosis and treatment of immune-related adverse events.*

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Implications for Nursing Practice: *Nurses play key roles in recognizing immune-related adverse events, providing patient education, and helping to facilitate interprofessional collaboration.*

Key Words: *immunotherapy, immune checkpoint inhibitors, interprofessional collaboration.*

Major breakthroughs in oncology drug development have expanded treatment options for cancer patients, heralding the era of precision cancer therapy. Often, these medications have unique adverse events that are not seen with traditional cytotoxic therapies and they may be unfamiliar to the oncology team. Interprofessional collaboration is critical to improve outcomes and manage patients effectively.

The field of immuno-oncology has seen rapid growth in recent years. Immunotherapy is one type of precision cancer treatment; it harnesses a person's own immune system to help fight cancer.[1] Immune checkpoint inhibitors are one type of immunotherapy; they have demonstrated impressive results in different cancer types and have produced durable responses in a subset of patients.[2-9] As use of immune therapy moves from academic medical centers to the community, it is important that providers understand drug mechanism of action, potential unique adverse events and their management. This article will focus on the roles of gastroenterology, endocrinology, and neurology in the interprofessional collaborative management of oncology patients receiving immune checkpoint inhibitors.

Immune Checkpoint Inhibitors: Indications and Mechanism of Action

Immune checkpoint inhibitors can help restore an immune response against tumors.[1] Several of these drugs were extensively tested in melanoma, with more recent expansion to other disease types. Ipilimumab (Yervoy, Bristol Myers Squibb, Princeton, NJ, USA) was the first immune checkpoint inhibitor approved by the US Food and Drug Administration (FDA) in 2011 based on demonstrated overall survival benefit compared with peptide vaccine in patients with advanced melanoma.[2] Ipilimumab is a recombinant, human monoclonal antibody that binds to the cytotoxic T-lymphocyte–associated antigen 4 (CTLA-4). This action blocks the interaction of CTLA-4 with its ligands and promotes T-cell activation and growth, including T-effector cells that infiltrate tumors. Blocking CTLA-4 can also reduce T-regulatory cell function, thereby improving T-cell responsiveness and the anti-tumor immune response.[1,10] Ipilimumab later gained FDA approval in 2015 for adjuvant therapy of high-risk stage III melanoma (defined as patients with melanoma involvement of regional lymph nodes of more than 1 mm who have undergone complete resection, including total lymphadenectomy); this approval was based on improved recurrence-free survival compared with observation in a large phase III trial.[11]

There have been five additional immune checkpoint inhibitors approved by the FDA in the past 3 years, including pembrolizumab (Keytruda, Merck and Co., Inc. Whitehouse Station, NJ, USA), nivolumab (Opdivo, Bristol Myers Squibb, Princeton, NJ, USA), atezolizumab (Tecentriq, Genentech, Inc., South San Francisco, CA, USA), avelumab (Bavencio, EMD Serono, Inc. and Pfizer, Inc., New York, NY, USA), and durvalumab (Imfinzi, AstraZeneca, Wilmington, DE, USA). Pembrolizumab is a humanized monoclonal antibody and nivolumab is a fully human monoclonal antibody; both are anti-PD-1 inhibitors. Some tumors can avoid being recognized by the immune system through the Programmed Death receptor-1 (PD-1) pathway because they express Programmed Death ligand (PD-L1) and Programmed Death ligand 2 (PD-L2) which bind with PD-1 receptors on T cells to inactivate them. Anti-PD-1 antibodies bind to the PD-1 receptor to block this interaction, thereby promoting T-cell activity and the immune response.[1,12-14]

Pembrolizumab was originally approved by the FDA for advanced or unresectable melanoma in 2014 for second-line use after ipilimumab (and, if BRAF V600E mutant, after BRAF inhibitors). It gained approval for first-line use in melanoma regardless of BRAF status in 2015 after demonstrating improved overall and progression-free survival compared with ipilimumab in a large phase III trial.[9]