Evaluation of immune checkpoint inhibitors in oncology
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Immune checkpoint inhibitors (ICIs) are utilized in oncology to stimulate the immune system and induce an anti-tumor response. The current pathways inhibited are cytotoxic T-lymphocyte associated antigen-4 (CTLA-4, ipilimumab), programmed death-1 (PD-1, nivolumab and pembrolizumab), and programmed death ligand 1 (PD-L1, atezolizumab).

ICIs have had rapid uptake into practice due to improved response rates, longer durations of response, and unique side effect profile compared to standard chemotherapy. Although the ICIs have lower grade 3 and 4 toxicities compared to traditional chemotherapy, they are associated with immune-mediated adverse effects in 14% (PD-1 inhibitors) to 60% (ipilimumab) of patients. However, their broad mechanism has made them attractive agents for a variety of malignancies, including non-FDA approved indications and for patients with few treatment options. The ICIs are costly, ranging from an average wholesale price of $75,000 for 6 months of a PD-1 inhibitor to $400,000 for a course of adjuvant ipilimumab. Due to their high cost, patients at Virginia Commonwealth University Health (VCUH) are required to have prior authorization or patient assistance program approval. However, providers are uncertain of the financial burden these agents place on patients, particularly for off-label indications.

A retrospective electronic medical record analysis reviewed all patients who received at least 1 dose of an ICI from January 1, 2012 to June 30, 2016. Exclusions included participation in a clinical trial, age < 18 years, pregnancy, and incarceration. The primary objective was to characterize the use of ICIs at VCUH, with a focus on frequency of off-label administration, survival from start of treatment, and adverse effects. Medication cost billed to patients was also assessed. This project will allow for a better understanding of use of ICI use, prescribing patterns, and patient financial burden.

Of the 133 patients evaluated, 48 received ipilimumab, 60 nivolumab, and 25 pembrolizumab. The median number of doses received was 3 for ipilimumab, 4.5 for nivolumab, and 5 for pembrolizumab. Treatment for an off-label indication occurred in 2% of ipilimumab, 25% of nivolumab and 24% of pembrolizumab patients. The average time from first treatment until death was 6 months with ipilimumab, 2 months with nivolumab, and 4 months with pembrolizumab.

Immune-mediated adverse effects occurred in 33% of ipilimumab patients, 15% of nivolumab patients, and 28% of pembrolizumab patients. The most common adverse effects were dermatologic and gastrointestinal. An emergency department visit or admission for immune-mediated adverse effects occurred in 25% of patients, with 22.6% requiring a dose delay and 51.6% requiring therapy discontinuation. Medication cost billed to the patient is still being collected and will be presented.