Treatment with vemurafenib, a selective BRAF inhibitor, has shown significant improvement in patient survival compared with standard therapy in BRAF V600-mutant metastatic melanoma. Similar studies have shown improvement using another BRAF inhibitor, dabrafenib mesylate. No cases of acute kidney injury (AKI) have been reported with dabrafenib use. Acute kidney injury has recently been reported in a few case series with vemurafenib use. One case series included a patient who had a kidney biopsy demonstrating acute tubular necrosis as a potential mechanism of renal injury.

**Methods**

A waiver of institutional review board review was received for this study. We reviewed the Food and Drug Administration Adverse Event Reporting System (FAERS) quarterly legacy data file from the third quarter of 2011 through second quarter of 2014 for vemurafenib and second quarter of 2013 through second quarter of 2014 for dabrafenib. Data regarding renal adverse events related to vemurafenib and dabrafenib therapy were extracted from the database through formation of a query using FAERS-assigned unique case identifiers. Search terms used were “renal insufficiency, elevated creatinine, renal failure, renal injury, proteinuria, renal impairment, blood creatinine increase, renal failure acute, low phosphorus, hypophosphatemia, hypercreatinemia, hyponatremia, hypokalemia, renal damage.”

**Results**

A total of 132 cases of AKI in patients receiving vemurafenib therapy were reported to the FAERS during the period reviewed. Eighty-five patients were men, and 47, women (P < .001). The mean age of the men was 65 years, and of the women, 59 years (P = .04). The cases were reported from around the world, with France, the United States, and Germany reporting most of the cases. Fourteen cases of electrolyte disorders were reported (6 cases of hypokalemia and 8 cases of hyponatremia). The most common indication was for treatment of malignant melanoma.

Thirteen cases of AKI in patients receiving dabrafenib therapy were reported to the FAERS during the period reviewed. Twelve patients were men. The mean age of the men was 55 years, and of the women, 75 years (P = .002). Eight cases of electrolyte disorders were reported (2 cases of hypokalemia...
mia and 6 cases of hyponatremia). Contrary to prior reports, no cases of hypophosphatemia were found.²

Discussion

Although the FAERS reporting system is an unsophisticated database with scant demographic information, the number of AKI cases reported with BRAF inhibitor therapy is still alarming. Vemurafenib appears to be more nephrotoxic than dabrafenib. This renal toxicity seems to be more prevalent among male patients with melanoma. On the basis of the few published case reports,¹ we believe that the mode of injury seems to be tubular interstitial injury. Proteinuria was not reported.

Conclusions

This FAERS reporting system signal of renal injury with BRAF inhibitor therapy is important because this class of drugs confers significant survival benefit in patients with melanoma. On the basis of our findings, there is a heightened need to monitor renal function and electrolyte levels in all patients who receive these drugs. Dermatologists, oncologists, and nephrologists need to be made aware of this potential hazard. Kidney biopsies are needed to elucidate the mechanism behind the toxicity. We urge large cancer centers to look into close follow-up of patients with renal injury from these agents and to determine outcomes.

REFERENCES