Acute and chronic kidney function decline in patients receiving BRAF inhibitors for melanoma

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ABSTRACT

Introduction: BRAF and MEK inhibitors are utilized in combination to treat BRAF V600E/K-mutant metastatic melanoma. Although the initial clinical trial data did not reveal a signal for nephrotoxicity, several recent reports highlight a high risk of acute kidney injury (AKI) patients treated with BRAF inhibitors. We aimed to characterize the risk of developing chronic kidney disease (CKD) in patients who received BRAF inhibitors.

Methods: We performed a retrospective cohort study to evaluate kidney outcomes in patients in the Mass General-Brigham healthcare system who received dabrafenib, encorafenib, or vemurafenib between 2010 and 2019 and survived at least two years compared to controls with early-stage melanoma who underwent surgical resection alone. Patients were matched using propensity score matching based on age, sex, race, baseline creatinine, and presence of significant comorbidities including hypertension and diabetes mellitus. The outcomes were AKI and a composite CKD outcome of >30% eGFR decline or new onset eGFR < 60 mL/min/1.73m² sustained for 90 days. Cox proportional-hazards modeling was used to calculate hazard ratios. The etiology of the composite CKD was determined for a subset of cases by chart review.

Results: Sixty patients who received BRAF inhibitors and survived two years were matched to controls (1:3). Patients treated with BRAF inhibitors were at increased risk for AKI (HR 6.13, 95% CI = 2.17 - 17.32, p = 0.0006), and a composite outcome of >30% eGFR decline and new onset CKD (HR 3.35 95% CI = 1.50 - 7.50, p = 0.003).

Conclusions: Patients receiving BRAF inhibitors are at increased risk for AKI and CKD compared to matched controls with early-stage melanoma treated with surgery alone.