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Impact of Metabolic Dysregulation on Pluvicto Toxicity in Metastatic Prostate Cancer Treatment

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Abstract

Purpose: Prostate cancer is the leading cause of cancer-related deaths among men in Western countries. Pluvicto ([177Lu]Lu-PSMA-617) is an FDA-approved radiopharmaceutical that treats prostate-specific membrane antigen–positive metastatic castration-resistant prostate cancer (PSMA-positive mCRPC). Though this drug has great success in improving outcomes, there is substantial interpatient variability in prostate cancer control. The effect of metabolic dysregulation may influence the response to Pluvicto and subsequent toxicity. We sought to determine if metabolic dysregulation alters Pluvictotoxicity.

Methods: A single-institution retrospective chart review was performed to evaluate prostate cancer patients given Pluvicto. Patients were prescribed 200 mCi of Pluvicto for six cycles. The drug was injected over one minute via the direct injection method followed by two saline flushes of the syringe. 98% of the drug has been delivered consistently with this technique. Patient characteristics collected included BMI, diabetes status, race, and socioeconomic status. Clinical variables collected were white blood cell (WBC) and platelet (PLT) levels at baseline and after each injection of Pluvicto. Patients were separated by BMI and diabetes status; percent reduction of these cohorts' WBC and PLT levels from baseline to after the fourth Pluvicto injection was calculated. Significance was calculated using a t-test, and $p < 0.05$ was considered statistically significant.

Results: Between 2022-2024, 70 patients were treated with Pluvicto at a single institution. The cohort mean age was 71, predominantly Caucasian (82.9%), and a minority of African American patients (10%). A sizable portion of patients were overweight or obese (78.6%), and a quarter had diabetes (25.7%). Insurance coverage varied, with 41.4% having private insurance and 54.3% covered by Medicare or Medicaid. Regarding WBC changes, normal-weight patients experienced a 17.9% reduction, while overweight or obese patients saw a more pronounced reduction of 31.1% (p=0.02). Non-diabetic patients had a 25.8% reduction in WBCs from baseline, compared to a 35.9% reduction in diabetic patients (p=0.88). When comparing normal-weight and non-diabetic patients to those who were both obese and diabetic, the reductions were 11.6% and 34.8%, respectively (p=0.31). For PLT changes, normal-weight patients had a 48.7% reduction, while overweight or obese patients had a 25.9% reduction (p=0.15). Non-diabetic and diabetic patients had almost identical reductions in PLT from baseline, 30.2% and 30.1%, respectively (p=0.81). Comparing normal-weight and non-diabetic patients to obese and diabetic patients, the reductions in PLT were 45.2% and 21.6%, respectively (p=0.32). This data illustrates considerable variability in WBC and PLT changes based on weight and diabetes status.

Conclusion: Our study found that patients with metabolic syndromes, including obesity and diabetes, may be prone to leukopenia following Pluvicto. After four cycles of Pluvicto, WBC counts decreased in most patients, but more profoundly for patients with metabolic dysregulation. Further investigation in larger data sets should be performed to determine if specific populations require Pluvicto dose reductions.