Title: *Balancing Oncologic Benefit and Allograft Survival: Cemiplimab for Metastatic Cutaneous Squamous Cell Carcinoma in a Kidney Transplant Recipient*

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Background: Immune checkpoint inhibitors (ICIs) have transformed the treatment of advanced cutaneous squamous cell carcinoma (cSCC). However, their use in kidney transplant recipients remains challenging due to the risk of acute allograft rejection. Strategies to balance oncologic benefit and graft preservation are still evolving.

Case Presentation: A 55-year-old woman underwent kidney transplantation 13 years earlier and had a history of cSCC treated with surgery and adjuvant radiotherapy. She subsequently presented with weight loss, anorexia, and fatigue. Investigation revealed right axillary lymphadenopathy, and biopsy confirmed metastatic cSCC. Brain imaging demonstrated multiple metastatic lesions. Following multidisciplinary discussion, treatment options and associated risks were reviewed with the patient. Immunosuppression was modified to corticosteroids and an mTOR inhibitor according to the Hanna protocol aimed at reducing rejection risk during ICI therapy. Cemiplimab and whole-brain radiotherapy were initiated. Three weeks after the first dose of cemiplimab, the patient developed severe acute allograft rejection, with serum creatinine rising from 1.8 to 8.0 mg/dL, nephrotic-range proteinuria (uACR 33 g/g), oliguria, and dialysis dependence. Despite intensive treatment with methylprednisolone, thymoglobulin, plasmapheresis, intravenous immunoglobulin, and hemodialysis, rejection remained refractory. Imaging demonstrated an enlarged renal allograft with heterogeneous enhancement suggestive of severe hypoperfusion. Graft nephrectomy was ultimately required. Despite allograft loss, the patient achieved meaningful oncologic benefit. At eight months of follow-up, she remains alive and clinically stable, exceeding the expected survival associated with metastatic cSCC without effective systemic therapy.

Conclusions: This case highlights the difficult balance between cancer control and graft preservation in kidney transplant recipients receiving ICIs. Even with modified immunosuppression, severe rejection may occur. However, the observed oncologic benefit supports consideration of ICIs in carefully selected transplant recipients facing otherwise limited therapeutic options.