

Renal function before and after cytoreductive nephrectomy in a phase 3 randomized clinical trial

Erik N. Mayer, BS*, William T. Lowrance, MD, MPH, Salt Lake City, UT, Robert Uzzo, MD, Philadelphia, PA, Christopher Wood, MD, FACS, Houston, TX, Alexander Kutikov, MD, FACS, Marc Smaldone, MD, MSHP, Philadelphia, PA, Jason Gee, MD, Burlington, MA, William Huang, MD, New York, NY, Thomas Gardner, MD, Indianapolis, IN, Gennady Bratslavsky, MD, Syracuse, NY, Jeff Holzbeierlein, MD, FACS, Kansas City, MO, Lawrence Karsh, MD, Denver, CO, Viraj Master, MD, PhD, FACS, Atlanta, GA, Neal Shore, MD, Myrtle Beach, SC, Brian Lane, MD, PhD, FACS, Grand Rapids, MI

INTRODUCTION AND OBJECTIVES: Cytoreductive nephrectomy (CN) in the setting of metastatic renal cell carcinoma (mRCC) has shown improvement in overall survival for select patients when combined with systemic therapy, but its impact on renal function is not completely understood. Our objective was to assess renal function before and after CN in patients with mRCC participating in the ADAPT (The Autologous Dendritic Cell Immunotherapy (AGS-003) Plus Standard Treatment of Advanced Renal Cell Carcinoma) trial.

METHODS: We examined pre-/post-CN renal function from the ongoing phase 3 clinical trial involving administration of AGS-003 + Sunitinib vs. Sunitinib alone after CN in patients with mRCC. Records of patients at trial sites between January 2013 and July 2015 were reviewed for tumor characteristics, established CKD risk factors, and demographic information. A univariate and multivariate logistic regression analysis was used to evaluate the impact of patient and disease specific factors on pre-operative renal function.

RESULTS: The ADAPT trial has enrolled >1000 patients at 113 centers worldwide since April 2012. Trial accrual completed mid-2015. Pre-operative info was available for 1007 patients. Of those undergoing CN, 198 (19.7%) had stage 3 or greater CKD (GFR < 60ml/min/1.73 m²) at baseline. Factors independently associated with an increased risk of pre-operative stage 3 or greater CKD included age at diagnosis (OR: 1.064, 95% CI: 1.042-1.087, p < .0001), LDH above the upper limit of normal (OR: 1.851, 95% CI: 1.231-2.781, p<0.003), and advanced tumor stage. The likelihood of having at least stage 3 CKD at surgery was lower for T stage 1 (OR 0.432, 95% CI: 0.192-0.969, p<0.042) and T stage 2 disease (OR: 0.303, 95% CI: 0.117-0.788, p<0.014) than for T stage 3. Gender, race, low albumin, symptoms of metastasis, and adenopathy were not significantly associated with pre-operative CKD stage 3 or greater. Post-operative GFR data was limited to 426 patients; the median change after CN was -21.6 ml/min/1.73 m². Of these patients, 160 (37.6%) developed CKD 3 or greater post CN in the setting of previously normal renal function.

CONCLUSIONS: The ADAPT trial is the largest randomized CN trial completed to date. Here we observed that one fifth of patients with mRCC in this trial had baseline stage 3 or worse CKD. Increasing tumor stage and age were associated with a greater risk for pre-operative CKD in patients undergoing CN. Moreover, 37.6% of patients with available data developed de novo CKD 3 or worse post-CN. Older patients with advanced disease may be at higher risk of significant renal insufficiency after CN.

Source of Funding: None