

Effects of GC4419 (Avasopasem Manganese) on Chronic Kidney Disease in Head and Neck Cancer Patients Treated with Radiation and Cisplatin

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Background

- Nephrotoxicity (acute or chronic) is a major complication of platinum-based chemotherapy in 31–68% of patients
- Platinum-induced chronic kidney disease (CKD) affects morbidity and mortality
- CKD is a risk for patients with head and neck cancer (HNC) treated with standard of care chemoradiotherapy with cisplatin (CRT)
- NCT02508389: randomized, multicenter, placebo-controlled Phase 2b trial of GC4419 (avasopasem manganese, 30 mg or 90 mg Monday–Friday x 7 weeks) in patients with HNC receiving CRT
 - N = 223: 40% received 100 mg/m² Q3W and 60% received 30–40 mg/m² QW
 - Avasopasem reduced duration, incidence, and severity of severe oral mucositis (Anderson, et al JCO 2019)
 - No difference in 1- or 2-year tumor control across study arms
 - No acute differences in kidney injury

Methods and Materials



85/223 trial patients received 3 cycles of 100 mg/m² cisplatin plus placebo or 30 mg or 90 mg avasopasem intravenously prior to RT



Of the 85 trial patients, a retrospective analysis of 52 patients:

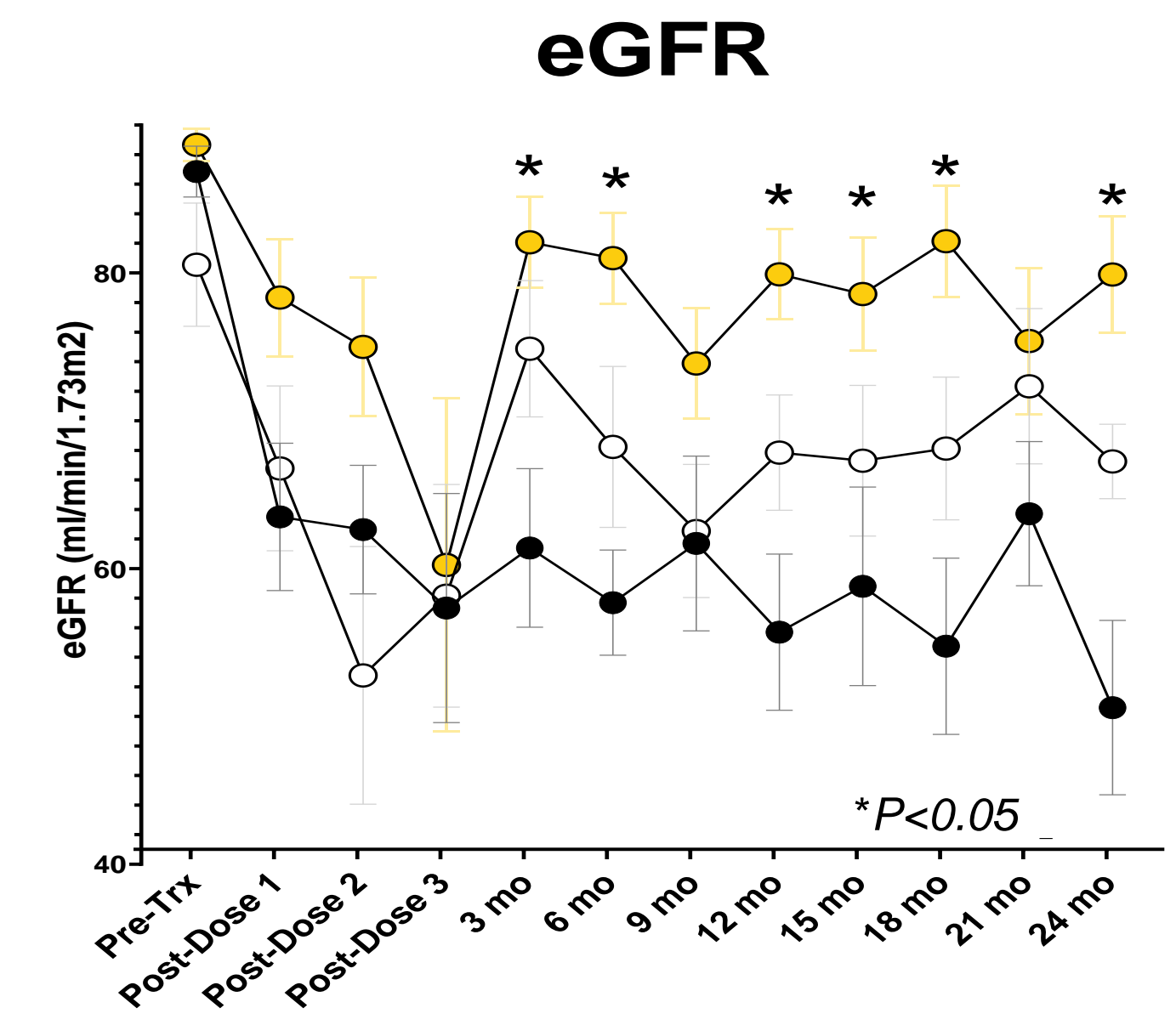
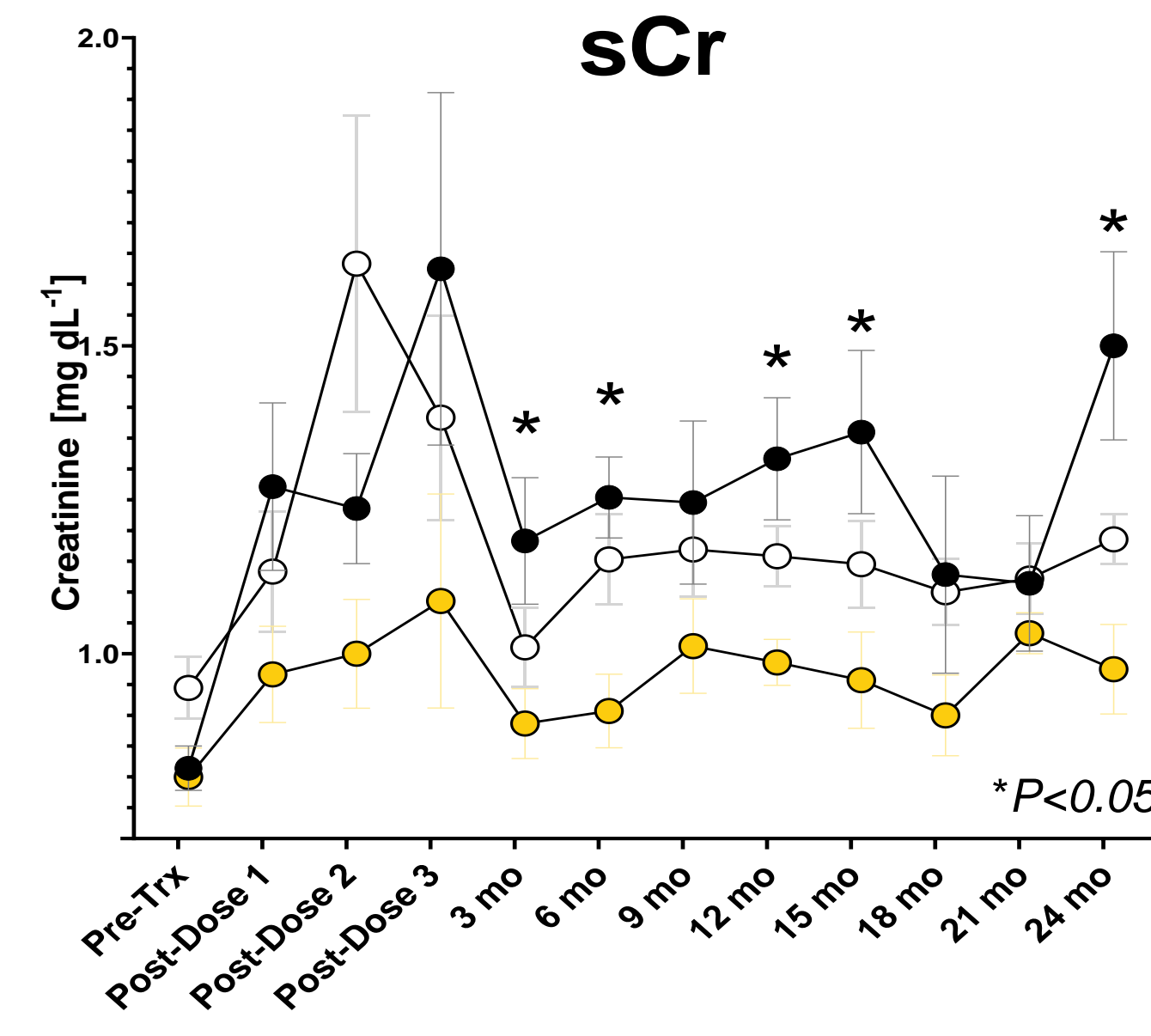
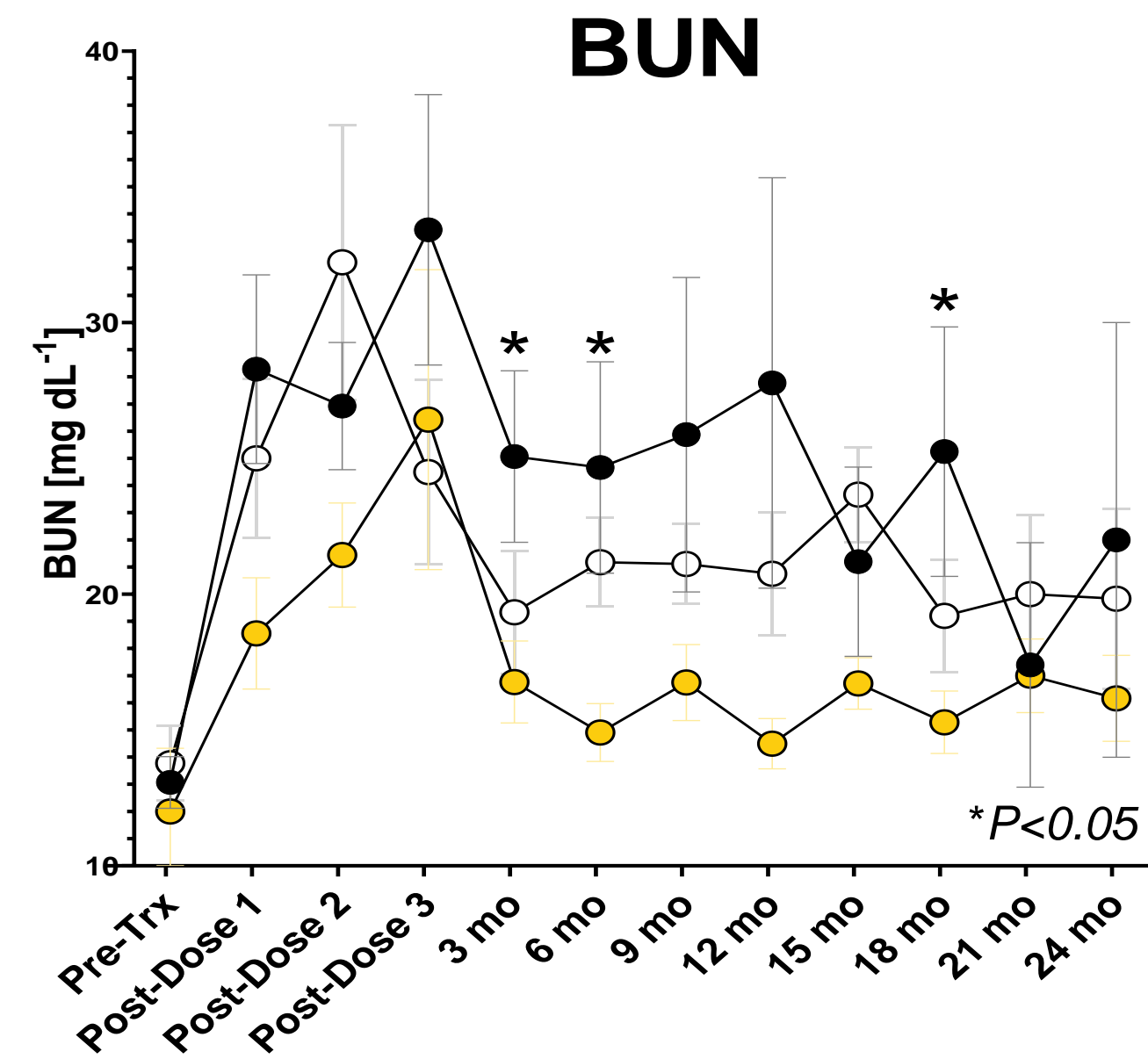
- 15/52 90 mg avasopasem (GC4419)
- 18/52 30 mg avasopasem (GC4419)
- 19/52 placebo + comparator (including 7 matched comparator patients who received the same CRT outside of the trial)



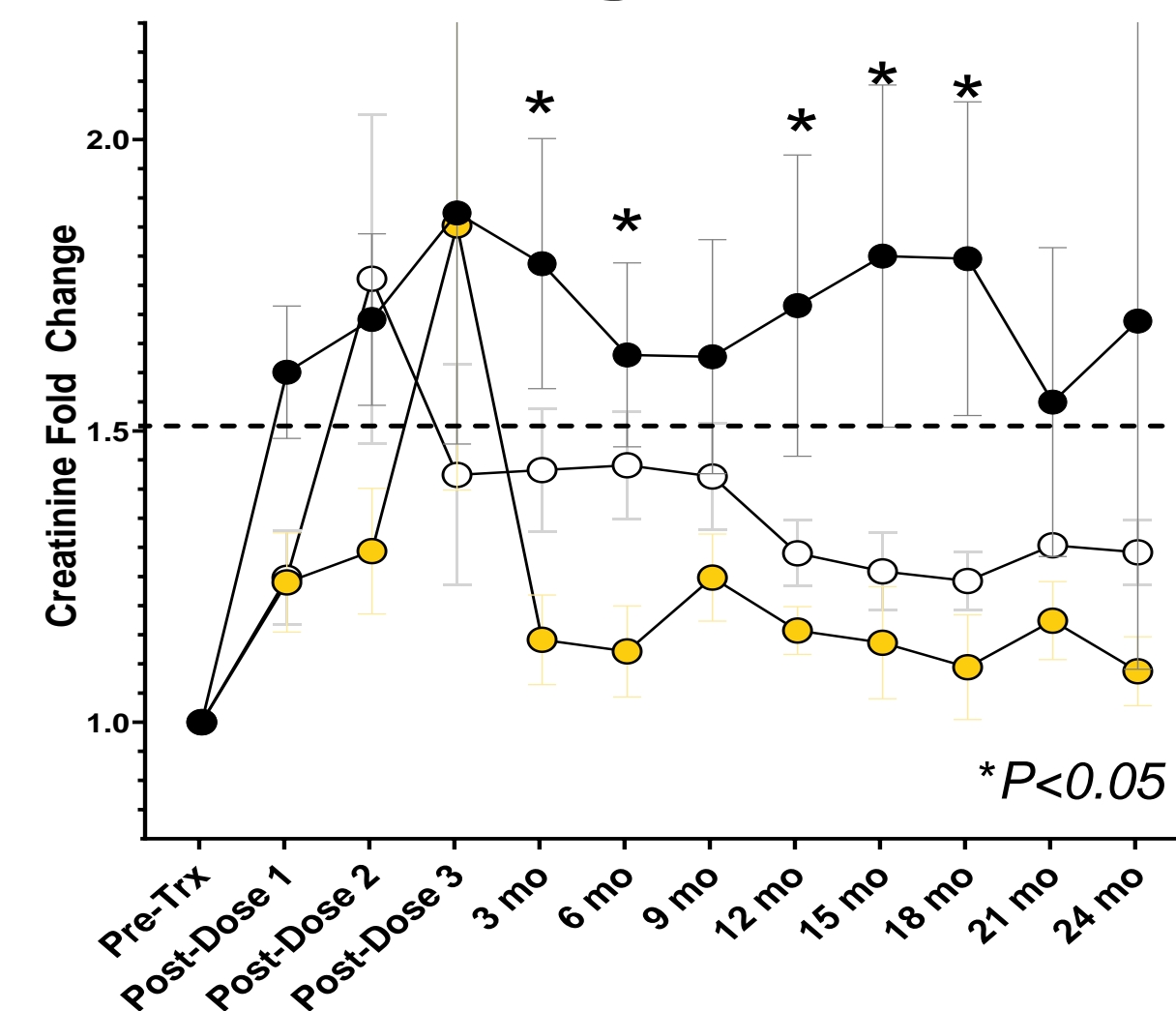
Kidney function evaluated between 3- and 24-months post-completion of CRT by blood urea nitrogen (BUN), serum creatinine (sCr), and estimated glomerular filtration rate (eGFR)

Assessment by two-way analysis of variance (ANOVA) as defined by the Kidney Disease Improving Global Outcomes (KDIGO) CKD staging

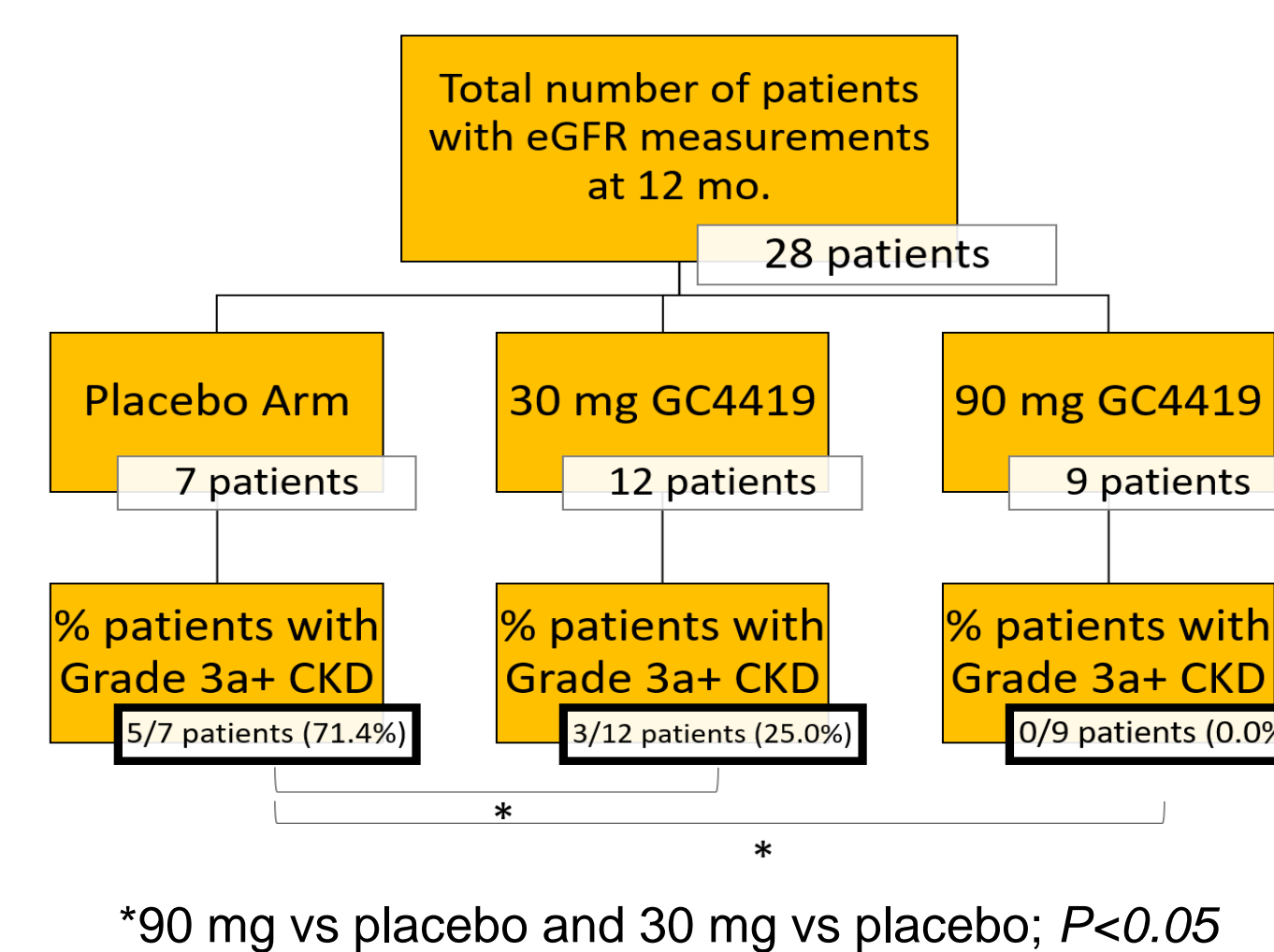
90-mg Avasopasem Arm Demonstrated a Return to Normal Kidney Function 24 Months After CRT



Change in sCr



eGFR Measurements at 12 Months



In this retrospective analysis, 90 mg Avasopasem:

- Normalized BUN and sCr post treatment
- Increased eGFR post treatment
- <1.5-fold increase in sCr versus baseline
- <25% decrease in eGFR versus baseline
- Fewer eGFR measurements <60 mL/min (stage G3a/b, G4, or G5 CKD)

Conclusion

- Avasopasem manganese (GC4419) may have the potential to reduce the incidence and severity of CKD in patients with HNC receiving concurrent radiotherapy with high-dose cisplatin
- Further evaluation of the effect of avasopasem on CKD is needed

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