

# One-year Reductions in Cisplatin-Related Chronic Kidney Disease (CKD) in Patients With Head and Neck (HNC) Cancer Treated With Avasopasem Manganese: A Prespecified Analysis From the Phase 3 ROMAN Trial

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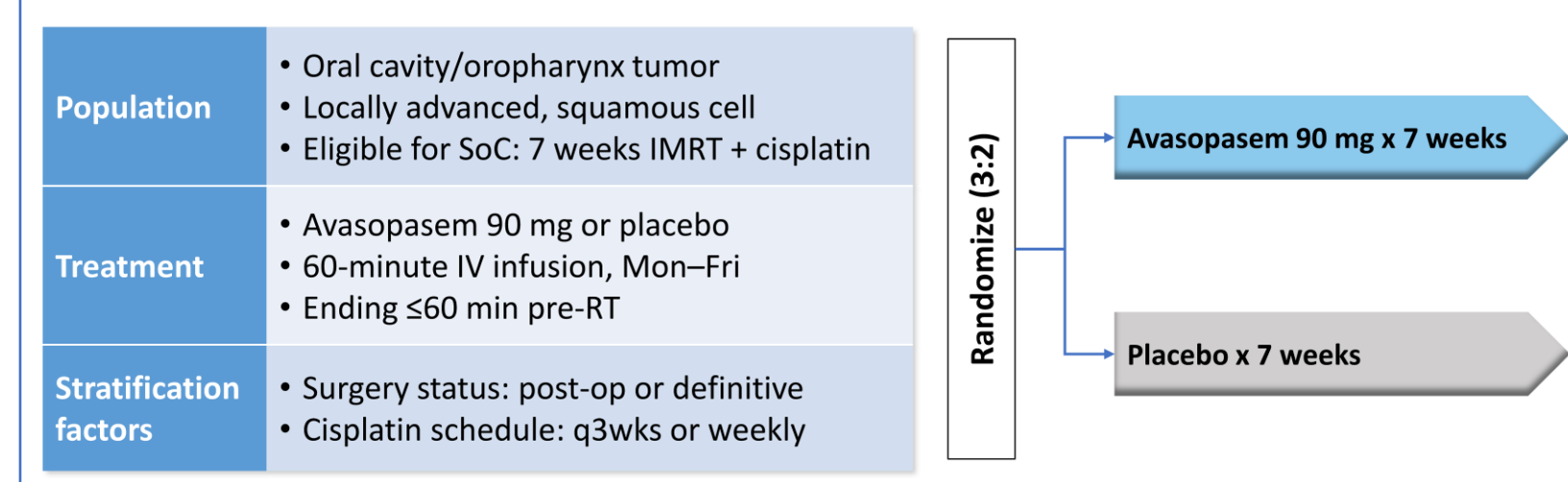
## Background

- Cisplatin-induced AKI, AKD, and CKD are caused by increased production of reactive oxygen species, notably superoxide, in conjunction with alterations in mitochondrial electron transport chain complex activities in renal tubules<sup>1,2</sup>
- These pathologies can be alleviated by increasing superoxide dismutase activity, which decreases superoxide<sup>1</sup>
- The investigational new drug avasopasem manganese, a selective dismutase mimetic, ameliorates cisplatin-induced kidney injury in murine models<sup>2</sup>
- Preclinical results demonstrate avasopasem does not interfere with cisplatin anticancer activity<sup>3</sup>
- Retrospective analysis of 1-year kidney function in a limited subset of patients treated in a randomized, placebo-controlled phase 2b trial of avasopasem to reduce SOM from CRT suggested avasopasem may preserve kidney function compared to placebo<sup>4</sup>

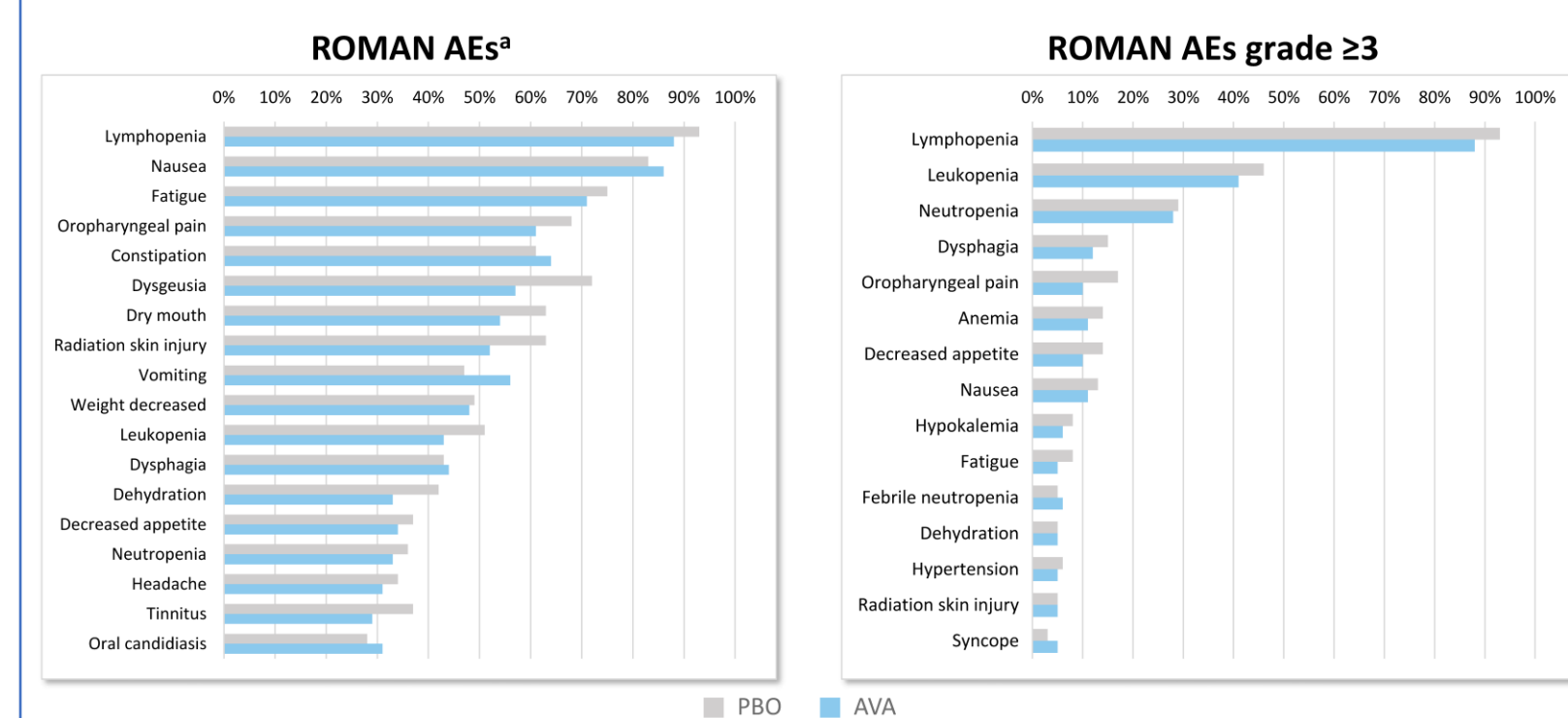
## GTI-4419-301: The ROMAN Trial (NCT03689712)

- ROMAN was a phase 3 randomized, placebo-controlled double-blind study of avasopasem for the reduction of SOM in patients with locally advanced, nonmetastatic HNC undergoing SOC CRT (**Figure 1**)
- Avasopasem in combination with CRT demonstrated meaningful reduction in SOM across multiple endpoints vs placebo (**Figure 2**), with adverse events comparable between treatment groups (**Figure 3**)<sup>5</sup>

**Figure 1. ROMAN Study Design and Eligibility Criteria**



**Figure 3. ROMAN Most Frequent Adverse Events**



<sup>a</sup>ITT population: 166 patients on placebo, 241 on 90 mg avasopasem.

**ABBREVIATIONS**  
AE, adverse event; AKD, acute kidney disease; AKI, acute kidney injury; AVA, avasopasem manganese; BUN, blood urea nitrogen; CKD, chronic kidney disease; CKD-EPI, CKD Epidemiology Collaboration; CRT, chemoradiation therapy; ECOG PS, Eastern Cooperative Oncology Group Performance Status; eGFR, estimated glomerular filtration rate; HNC, head and neck cancer; HPV, human papillomavirus; IMRT, intensity-modulated radiation therapy; ITT, intent to treat; IV, intravenous; MMRM, mixed-effects model repeated measures; OM, oral mucositis; PBO, placebo; Q3W, once every 3 weeks; QW, once every week; RT, radiation therapy; SAE, serious AE; sCr, serum creatinine; SD, standard deviation; SOC, standard of care; SOM, severe OM; Tx, treatment.

**REFERENCES**  
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## Results

### Patient Population

- ROMAN phase 3 trial ITT population: 407 patients
  - Avasopasem (N=241) vs placebo (N=166)
- Baseline patient characteristics were balanced between treatment groups (**Table 1**)

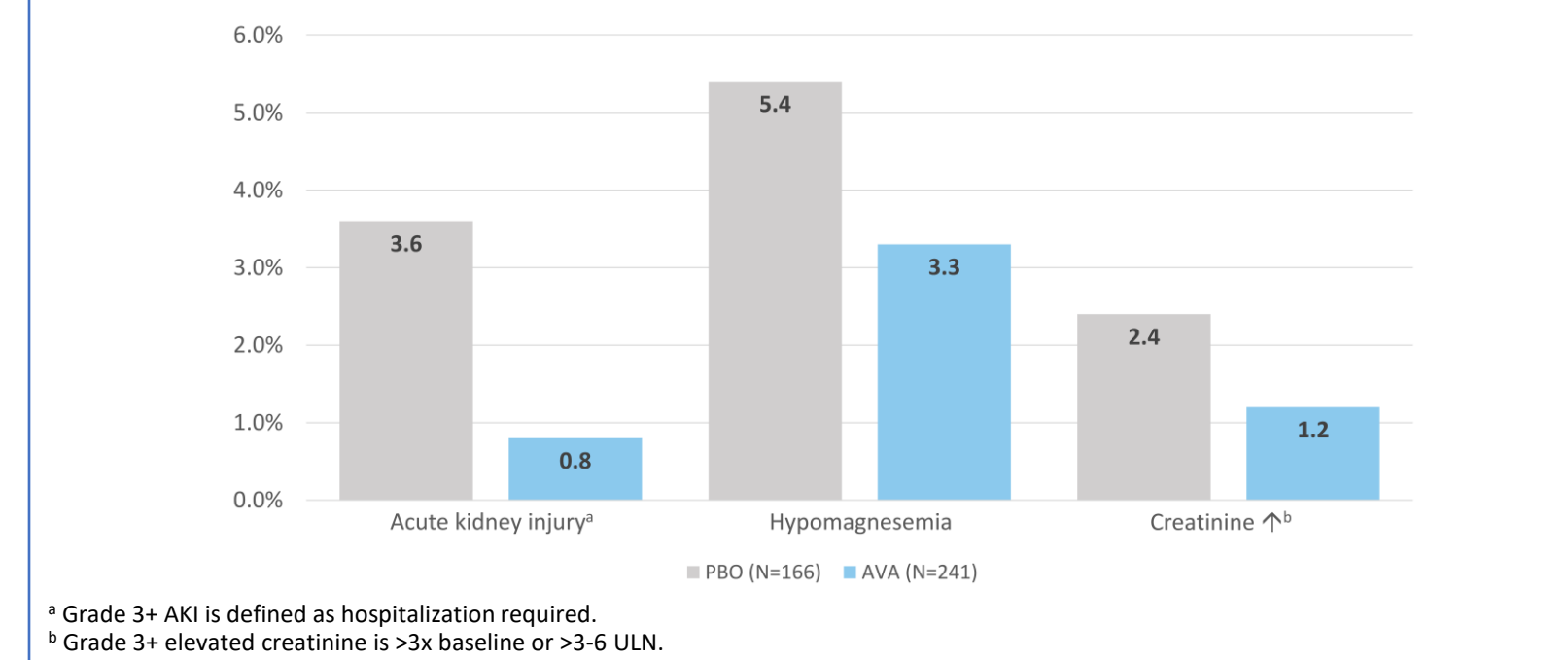
**Table 1. Patient Characteristics**

Characteristic	AVA 90 mg (n=241)	PBO (n=166)	All patients (N=407)
Sex, n (%)			
Male	202 (84)	149 (90)	351 (86)
Female	39 (16)	17 (10)	56 (14)
Age, years			
Mean (SD)	60.4 (9.37)	61.2 (8.64)	60.8 (9.08)
Median (range)	61 (32-81)	61 (34-84)	61 (32-84)
ECOG PS, n (%)			
0	186 (77)	115 (69)	301 (74)
1	54 (22)	50 (30)	104 (26)
2	1 (<1)	1 (1)	2 (<1)
Tumor site, n (%)			
Oropharyngeal	194 (80)	141 (85)	335 (82)
Oral cavity	38 (16)	21 (13)	59 (14)
Unknown	9 (4)	4 (2)	13 (3)
Treatment type, n (%)			
Definitive	195 (81)	134 (81)	329 (81)
Postoperative	46 (19)	32 (19)	78 (19)
Cisplatin schedule, n (%)			
Every 3 weeks	102 (42)	74 (45)	176 (43)
Weekly	139 (58)	92 (55)	231 (57)

### Renal Outcomes From ROMAN

- Reduced incidence of cisplatin-related renal adverse events during treatment with avasopasem (**Figure 4**)

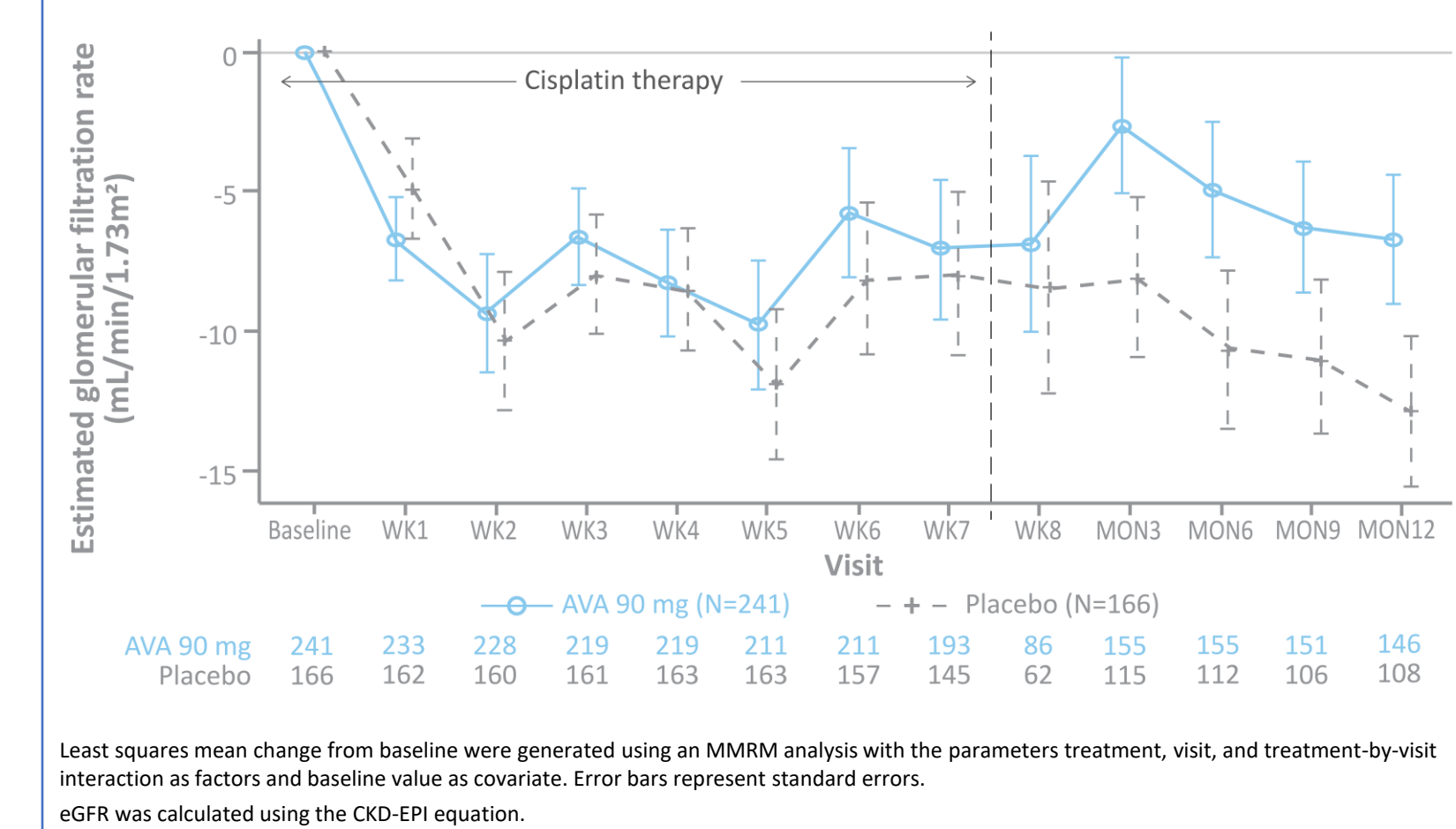
**Figure 4. Cisplatin Renal Grade 3+ AEs**



<sup>a</sup> Grade 3+ AKI is defined as hospitalization required.  
<sup>b</sup> Grade 3+ elevated creatinine is >3x baseline or >3-6 ULN.

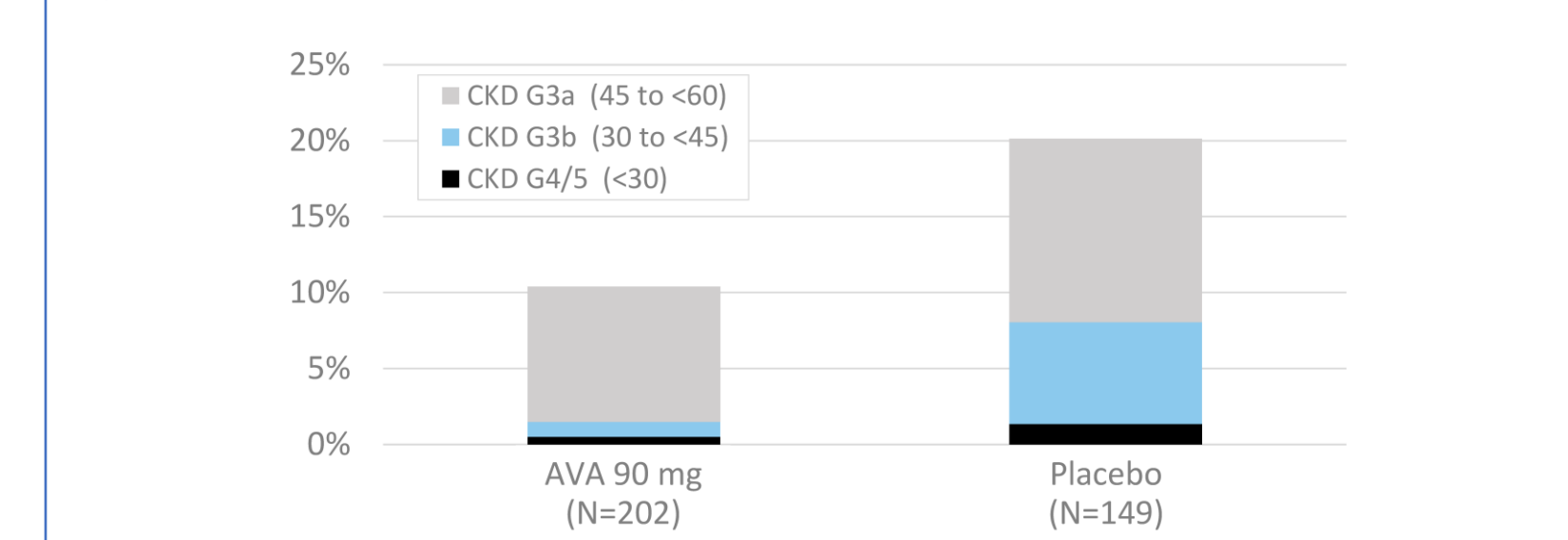
- Lesser mean reduction from baseline in eGRF with avasopasem (**Figure 5**)
- Significant improvements in preservation of eGFR (p=0.0008) with avasopasem compared to placebo

**Figure 5. Mean Change in eGFR From Baseline by Visit**



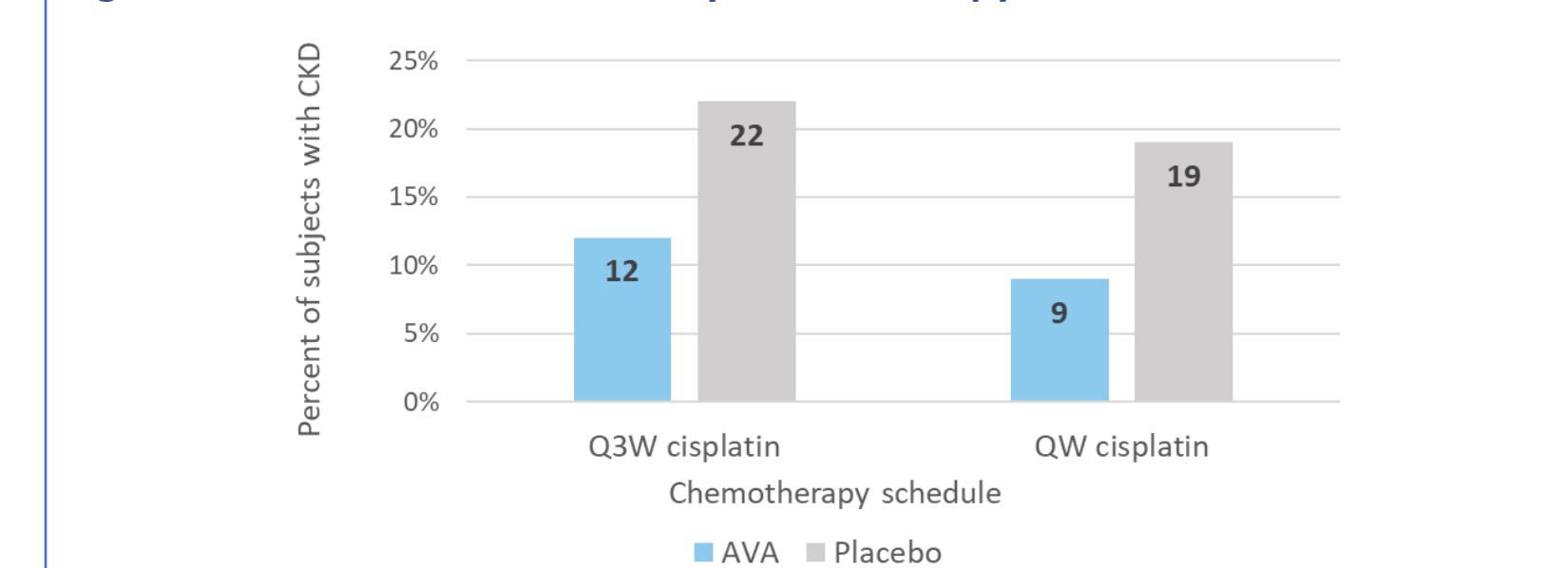
- Significant reduction in incidence of grade 3+ CKD according to KDIGO criteria (eGFR <60 mL/min/1.73m<sup>2</sup>) at 1-year follow-up with avasopasem compared to placebo (relative risk 0.55, p=0.0043, **Figure 6**)

**Figure 6. Grade 3+ CKD According to KDIGO Criteria at 1 Year**



- Reduced incidence of grade 3+ CKD with avasopasem among patients receiving Q3W therapy and for patients receiving QW therapy (**Figure 7**)

**Figure 7. Grade 3+ CKD at 1 Year by Chemotherapy Schedule**



## Conclusions

- Avasopasem appears to reduce cisplatin-related kidney damage in the study population during treatment and through 1-year follow-up
- Study results carry significance beyond CRT for HNC and may potentially impact platinum-containing regimens in other cancers; further research is required