Background
Non-clear cell renal cell carcinoma (nccRCC) represents around 25% of RCC variants. However, most data about use of nivolumab and ipilimumab (nivo-ipi) in kidney cancer comes from one trial in clear cell RCC (ccRCC).1 In a recent post-marketing study, CheckMate-920, involving 46 patients with nccRCC, nivo-ipi had an objective response rate (ORR) of 19.6%.2 Here, we aim to report real world experience with combination nivo-ipi in nccRCC.

Methods
Between 2017 and 2022, 48 patients (pts) with nccRCC were treated with nivo-ipi at our center. Toxicity, ORR and overall survival (OS) were retrospectively evaluated. Response was assessed by two board-certified radiologists. Median OS and follow up were calculated from the start of nivo-ipi using the Kaplan-Meier method. 95% confidence interval was calculated using the Clopper-Pearson Method.

Results
The majority of patients (92%) received nivo-ipi as first-line therapy and 40% had prior nephrectomy. Histological variants included: papillary (35%), chromophobe (19%), and unclassified (46%) (table 1). 33% of pts had sarcomatoid features (SF). ORR was 41% for papillary, 22% for chromophobe, and 32% for unclassified. Response among pts with SF was 12/16 (75%). Median follow-up from nivo-ipi start was 27.2 months (mo) (95% CI: 17.5–38.7). Median OS was 25.7 mo (95% CI: 11.9–54.8) months, with 54.8 mo (95% CI: 12.7–54.8) for papillary, 28.3 mo (95% CI: 0.6–Undefined) for chromophobe, and 11.9 mo (95% CI: 3.2–Undefined) for unclassified. Among patients with unclassified variants, median OS was improved for patients with presence of SF versus those without (HR=0.10; 95% CI: 0.03–0.33; p = 0.005). 31% of pts developed Grade 3–4 toxicity with pneumonitis (n=5), colitis (n=3), hepatitis (n=3), immune-mediated glomerulonephritis (n=2), rash (n=1), pancreatitis (n=1), ITP (n=1), and anaphylaxis (n=1). There were no reported Grade 5 toxicities.

Conclusions
Nivo-ipi demonstrated a favorable efficacy/toxicity profile in nccRCC, especially among the papillary variant. Pts with unclassified variant without SF had a high upfront PD rate and low median OS. Consistent with ccRCC, SF enriched for clinical benefit from nivo-ipi in nccRCC. Understanding the driving immune biology of nccRCC is necessary for optimizing the use of novel therapy combinations.

REFERENCES