523 NIVOLUMAB AND IPILIMUMAB IN PATIENTS WITH METASTATIC NON-CLEAR CELL RENAL CELL CARCINOMA AT MD ANDERSON CANCER CENTER

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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 (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 varient. 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.

Abstract 523 Table 1

Outcomes (%)	Papillary (N=17)	Chromophobe (N=9)	Unclassified (N=22)
Objective Response Rate (ORR) (95% CI)	7 (41%) (CI 21.6% – 63.9%)	2 (22%) (CI 6.3% - 54.7%)	7 (32%) (CI 16.3% - 52.6%)
Complete Response (CR)	0 (0%)	0 (0%)	1 (5%)
Partial Response (PR)	7 (41%)	2 (22%)	6 (27%)
Stable Disease (SD)	3 (18%)	3 (33%)	0 (0%)
Progressive Disease (PD)	4 (24%)	3 (33%)	12 (55%)
Sarcomatoid features	4 (51%)	4 (44%)	8 (36%)
ORR Among Sarcomatoid Features (95% CI)	4 (100%) (CI 51% – 100%)	2 (50%) (CI 15% – 85%)	6 (75%) (CI 40.9% – 92.9%)
Clinical Benefit (SD > 6mo, CR, PR)	10 (59%)	5 (56%)	7 (32%)
Median OS from nivo-ipi start, months (95% CI)	54.8 (12.7-54.8)	28.3 (0.6-Undefined)	11.9 (3.2-Undefined)

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