Real world outcomes of first line (1L) nivolumab and ipilimumab (NIVO IPI) in metastatic renal cell carcinoma (mRCC): an update from the International mRCC Database Consortium (IMDC)

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Background

- NIVO IPI is the only doublet immunotherapy combination currently approved for advanced mRCC and is one of several 1L options
- NIVO IPI was approved based on Checkmate214 (CM214) which was compared sunitinib in the 1L setting. It demonstrated a superior overall survival [56 vs 38 months], progression free survival [11.6 vs 8.4 months, and response rate [42% vs 27%]
- In most jurisdictions, NIVO IPI is only funded for intermediate- and poor-risk IMDC classification patients based on CM 214 because favorable risk pts had lower response rates and PFS.
- This study was designed to evaluated the real-world efficacy of 1L NIVO IPI using the IMDC, including patients with non clear cell RCC, and RCC with a sarcomatoid component

Methods

- A retrospective analysis of the IMDC was performed on all patients receiving 1L NIVO IPI for mRCC
- Outcome measures of interest were:
  - Overall survival (OS)
  - Time to treatment discontinuation (TTD)
  - Time to next treatment (TTNT; measured as time from 1L initiation to next treatment or censored if no second line treatment initiated)
  - Overall response rate (ORR)
- Conditional survival analysis were performed at 6- and 12-month landmarks

Results

- We identified 1145 patients with mRCC who received 1L NIVO IPI, with a median follow up time of 20 months
- At time of analysis, 873/1145 (73%) had stopped 1L NIVO IPI and 363/1145 (32%) were deceased
- Immune mediated adverse events were documented in 274/572 (48%) of patients

Conclusions

- This real-world dataset shows activity of 1L NIVO IPI across multiple subgroups including patients with favourable risk disease, non clear cell RCC, and sarcomatoid histology.
- Favorable risk patients should be interpreted with caution as these are highly selected in the real world (e.g. clinical trials patients, high selected pts treated off label)
- Sarcomatoid mRCC outcomes have remarkable effectiveness.
- The conditional survival analysis shows meaningful durable survival benefits for patients who remain alive and on immunotherapy beyond 6- and 12- months

Table 1: Key Outcomes of 1L NIVO IPI by Subgroup

1L NIVO IPI Clinical Outcome	All IMDC risk category				IMDC Intermediate/Poor			
	Overall[1]	Favourable[2]	Intermediate	Poor	All[1]	Clear Cell component	Non clear cell	Sarcomatoid
Median OS (mon) (95% CI)	41.4 (37.2-49.4) N=1137	47.8 (40.8-93.0) N=94	51.1 (44.4-NR) N=559	18.3 (13.9-26.3) N=313	40.2 (32.9-49.4) N=872	48.1 (37.4-53.5) N=621	29 (16.6-NR) N=110	53.4 (22.3-NR) N=116
	P=<0.0001							
Median TTD (mon) (95% CI)	4.6 (4-5.6) N=1113	6.5 (4.3-13.6) N=94	5.7 (4.6-7.1) N=559	3.6 (2.8-5.5) N=313	4.8 (4-5.9) N=848	5.7 (4.6-7.1) N=611	3.9 (2.8-6.7) N=109	8.3 (5.1-10.8) N=116
	P=0.0024							
Median TTNT (mon) (95% CI)	11.3 (10.1-13) N=1137	24.3 (14.3-38.1) N=94	11.8 (10.1-15.2) N=559	8.2 (6.4-10.1) N=313	10.2 (9.2-11.8) N=870	11.7 (9.8-13.9) N=619	7.4 (5.7-11.1) N=109	11.8 (9.1-17.2) N=116
	P=<0.0001							
ORR % (n/n)	38% (368/960)	37% (31/84)	41% (199/488)	35% (91/258)	39% (290/746)	42% (225/540)	34% (32/94)	50% (53/105)
	P=0.319532							

1. Includes all patients including those with missing data precluding IMDC risk classification and/or pathological classification
2. Interpret with caution as the use of NIVO IPI in IMDC Favourable disease was highly selected in the real world
mon= months, 95%CI= 95% confidence interval, NR= not reached

Table 2: Baseline Characteristics (All Patients)

Gender	
Male	836/1145 (73%)
Female	309/1145 (27%)
Age >/70 Years Old	
Yes	267/1145 (23%)
No	878/1145 (77%)
Clear Cell Component	
Yes	818/962 (85%)
No	144/962 (15%)
Sarcomatoid Features?	
Yes	162/962 (16%)
IMDC Classification	
Favourable	94/966 (10%)
Intermediate	559/966 (58%)
Poor	313/966 (32%)
Hypercalcemia	
Yes	147/979 (15%)
Anemia	
Yes	582/1021 (57%)
Neutrophils High	
Yes	151/1023 (15%)
Platelets High	
Yes	220/1040 (21%)
Diagnosis to Treatment Interval < 1 Year	
Yes	825/1132 (73%)
Karnofsky Performance Status <80%	
Yes	169/1045 (16%)
More than One Metastatic Site	
Yes	825/992 (83%)
Second Line Treatment (Any)	438/727 (60%)
Sunitinib	187 (25%)
Cabozantinib	140 (19%)
Pazopanib	60/504 (8%)

Table 3: Conditional Survival Analysis(All Patients)

If survived …	Then % chance of surviving additional time below…	
	1 year	2 years
6 months	81%	68%
12 months	81%	68%
If on NIVO IPI for …	**Then % chance of surviving additional time below…**	
	1 year	2 years
6 months	91%	76%
12 months	94%	84%

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