Characterizing IMDC prognostic groups in contemporary first-line combination therapies for metastatic renal cell carcinoma (mRCC)

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Background

- The combination of immuno-oncology agents (IO) ipilimumab and nivolumab (IPI-NIVO) and combinations of IO with vascular endothelial growth factor targeted therapies (IOVE) have demonstrated efficacy in clinical trials for the first-line treatment of mRCC[1-5]
- This study seeks to establish real-world clinical benchmarks based on the International mRCC Database Consortium (IMDC) risk criteria using vascular endothelial growth factor targeted therapy (VEGF-TT) treated patients for context

Methods

- The IMDC database (IMDConline.com) was used to identify patients with mRCC who received first-line IPI-NIVO, IOVE and VEGF-TT from 2002-2021
  - IOVE included axitinib/pembrolizumab, lenvatinib/pembrolizumab, cabozantinib/nivolumab, or axitinib/avelumab
  - VEGF-TT included sunitinib or pazopanib
- The primary endpoint was overall survival (OS) and was calculated from time of initiation of first-line therapy to death from any cause
- Log-rank tests were conducted to differentiate between favorable, intermediate, and poor risk OS outcomes within treatment groups
- Overall response rates (ORR) and complete response (CR) rates were calculated based on physician assessment of best clinical response.

Results

- 692 patients received IPI-NIVO, 224 received IOVE, and 7152 received VEGF-TT
- Baseline characteristics for IPI-NIVO, IOVE, and VEGF-TT, respectively, were as follows: median age (interquartile range) 63 (56-69), 64 (57-70), and 63 (56-70); male 72%, 74%, and 72% (P=0.74); non-clear cell histology 15%, 10%, and 13% (p=0.15); sarcomatoid features 24%, 15%, and 13% (P < 0.0001); brain metastasis 8%, 4%, and 8% (P=0.04); liver metastasis 18%, 14%, and 18% (p=0.17); underwent nephrectomy 61%, 79% and 80% (P < 0.0001).

Conclusions

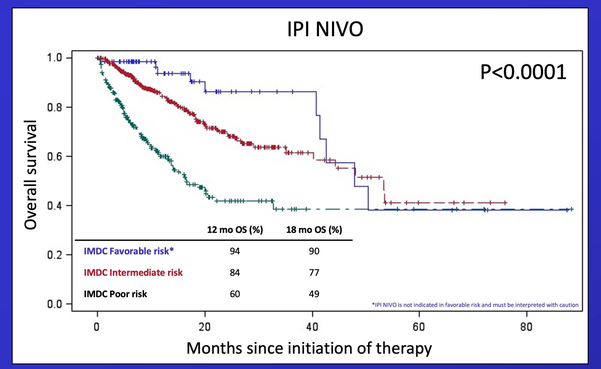
- IMDC criteria continue to risk stratify patients in contemporary combination therapies
- These findings provide real-world survival and response benchmarks for contemporary first-line mRCC treatments
- These findings may be useful for patient counseling and future trial development

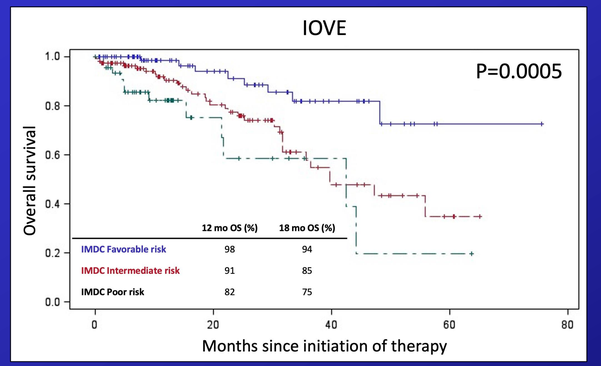
Table 1: Benchmark OS and response rate by IMDC risk group

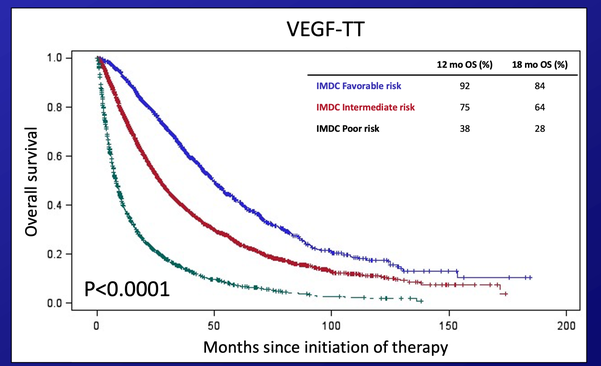
	IPI-NIVO n=692			IOVE n=244			VEGF-TT n=7152		
IMDC Risk	Favorable*	Intermediate	Poor	Favorable	Intermediate	Poor	Favorable	Intermediate	Poor
n (%)	66 (10)	399 (58)	227 (33)	81 (33)	117 (48)	46 (19)	1290 (18)	3977 (56)	1185 (17)
12-month OS	94%	84%	60%	98%	91%	82%	92%	75%	38%
18-month OS	90%	77%	49%	94%	85%	75%	84%	64%	28%
CR (%)	4/55 (7)	16/342 (5)	4/186 (2)	5/72 (7)	4/100 (4)	0/39 (0)	39/1160 (3)	121/3446 (4)	23/1529 (2)
ORR (%)	24/55 (44)	139/342 (41)	61/186 (33)	44/72 (61)	59/100 (59)	17/39 (44)	456/1160 (39)	1156/3446 (34)	320/1529 (21)

P-values (log rank) for OS between risk groups were significant for IPI-NIVO, IOVE, and VEGF-TT with p<0.001
*IPI-NIVO is not indicated in favorable risk patients and must be interpreted with caution

Table 2: OS Kaplan Meier curves







References

1. Powles T *et al.* Pembrolizumab plus axitinib versus sunitinib monotherapy as first-line treatment of advanced renal cell carcinoma (KEYNOTE-426): extended follow-up from a randomised, open-label, phase 3 trial. Lancet Oncol. 2020 Dec;21(12):1563-1573
2. Motzer RJ *et al.* Nivolumab plus Ipilimumab versus Sunitinib in Advanced Renal-Cell Carcinoma. N Engl J Med. 2018 Apr 5;378(14):1277-1290
3. Motzer R *et al.* Lenvatinib plus Pembrolizumab or Everolimus for Advanced Renal Cell Carcinoma. N Engl J Med. 2021 Apr 8;384(14):1289-1300
4. Choueiri TK *et al.* Nivolumab plus Cabozantinib versus Sunitinib for Advanced Renal-Cell Carcinoma. N Engl J Med. 2021 Mar 4;384(9):829-841
5. Motzer RJ *et al.* Avelumab plus Axitinib versus Sunitinib for Advanced Renal-Cell Carcinoma. N Engl J Med. 2019 Mar 21;380(12):1103-1115

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