Application of IMDC Criteria Across First-Line (1L) and Second-Line (2L) Therapies in Metastatic Renal-Cell Carcinoma (mRCC): New and Updated Benchmarks of Clinical Outcomes

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Background

- In patients with mRCC, the International mRCC Database Consortium (IMDC) criteria have been validated as a prognostic tool in a variety of settings, including:
  - 1L – 4L VEGF targeted therapy (VEGF TT)
  - 2L – 4L Nivolumab
  - Non-clear cell histologies (papillary and chromophobe RCC)
- In recent years, three 1L immuno-oncology (IO) combination therapies have been approved for use in mRCC:
  - Ipilimumab + Nivolumab (Ipi + Nivo)
  - Axitinib + Pembrolizumab (Axi + Pembro)
  - Axitinib + Avelumab (Axi + Avel)
- It is unknown whether the IMDC criteria can be used to risk stratify in recently approved 1L IO combination therapies.
- We sought to assess the ability of the IMDC criteria to risk stratify with the use of 1L IO combinations and provide updated benchmarks for older 1L and 2L treatments.

Methods

- Patients with mRCC starting systemic therapy between 2010-2019 were identified through the IMDC.
- IMDC risk score was calculated at the time of starting the line of therapy of interest.
- The primary endpoint was overall survival (OS) from time of initiating the treatment of interest.

Results

- A total of 6879 unique patients were included in the analysis.
  - 6379 treated in the 1L setting
  - 3577 treated in the 2L setting
- Baseline characteristics across the entire cohort are presented in Table 1.
- IMDC Criteria appropriately risk stratified into 3 prognostic groups in 1L IO combinations, in addition to older treatments (Table 2 / Figures 1-6).

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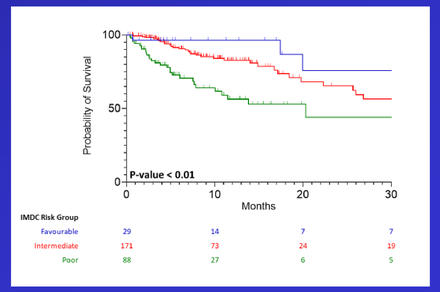
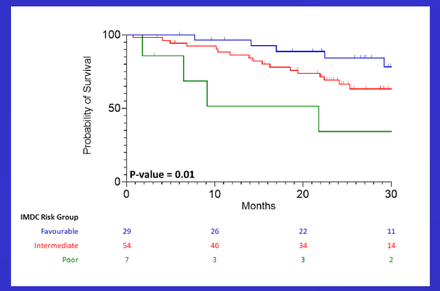
Figures 1-6: Application of IMDC Criteria Across 1L and 2L Therapies in mRCC

First Line Therapies

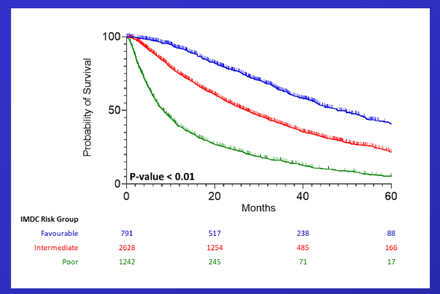
Ipilimumab + Nivolumab



Axitinib + Pembro / Avel

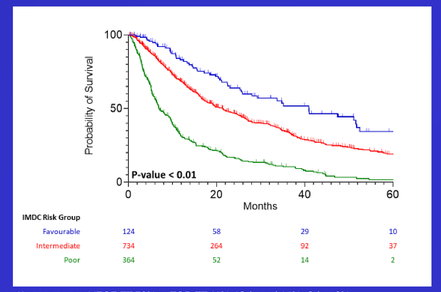


VEGF TT



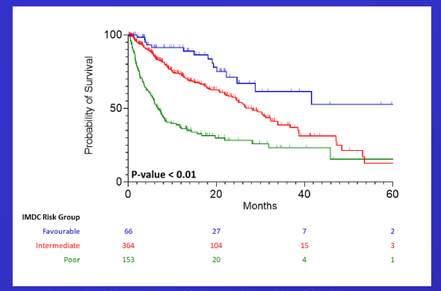
Second Line Therapies

VEGF TT



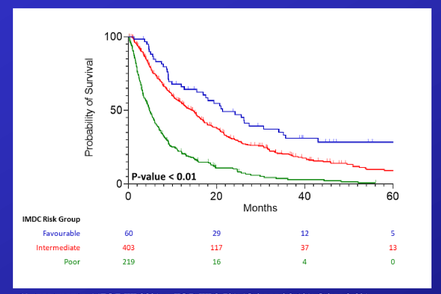
1L treatments: VEGF-TT 72%; mTOR-TT 11%; IO-based 14%; Other 3%

Nivolumab



1L treatments: VEGF-TT 95%; mTOR-TT 1%; IO-based 2%; Other 2%

Everolimus



1L treatments: VEGF-TT 99%; mTOR-TT 0.5%; IO-based 0.1%; Other 0.6%

Table 1: Baseline Characteristics and IMDC Risk Factors

	N = 6879
Age, median (IQR)	61 (53-68)
Male	4976 / 6879 (72%)
ccRCC	5509 / 6263 (88%)
Nephrectomy	5374 / 6868 (79%)
Sarcomatoid Features	797 / 4951 (16%)
1L IMDC Risk Groups	
Favourable	849 / 5061 (17%)
Intermediate	2867 / 5061 (57%)
Poor	1345 / 5061 (27%)
2L IMDC Risk Groups	
Favourable	250 / 2511 (10%)
Intermediate	1514 / 2511 (60%)
Poor	747 / 2511 (30%)

Table 2: Application of IMDC Criteria Across 1L and 2L Therapies in mRCC

	Favourable-Risk	Intermediate-Risk	Poor-Risk	P-value (log-rank)
	Median OS (months) by IMDC Risk Group			
1L VEGF TT† (N=5942)	47.8	27.2	8.3	<0.01
2L VEGF TT‡ (N=1687)	41.0	21.4	7.0	<0.01
2L Nivolumab (N=783)	NR	28.2	6.7	<0.01
2L Everolimus (N=1107)	21.4	14.7	4.8	<0.01
	Landmark OS by IMDC Risk Group*			
1L Ipi + Nivo (N=344)				
1-year OS	96%	83%	56%	<0.01
2-year OS	76%	65%	44%	
1L Axi + Pembro/Avel (N=93)				
1-year OS	96%	86%	51%	0.01
2-year OS	84%	69%	34%	

†Sunitinib, Pazopanib, Cabozantinib; ‡Sunitinib, Pazopanib, Cabozantinib, Axitinib, Lenvatinib; NR = Not Reached
*Due to the novelty of 1L IO combinations, median follow up time was shorter and thus landmark OS values are presented.

Conclusions

- IMDC criteria may be used to risk stratify in recently approved 1L IO combination therapies, in addition to older 1L and 2L treatments.
- These data provide contemporary benchmarks for OS that may be used for patient counseling and trial design.

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