Outcomes of First-line Immuno-oncology Combination Therapies in Metastatic Renal Cell Carcinoma: Results from the International Metastatic Renal Cell Carcinoma Database Consortium

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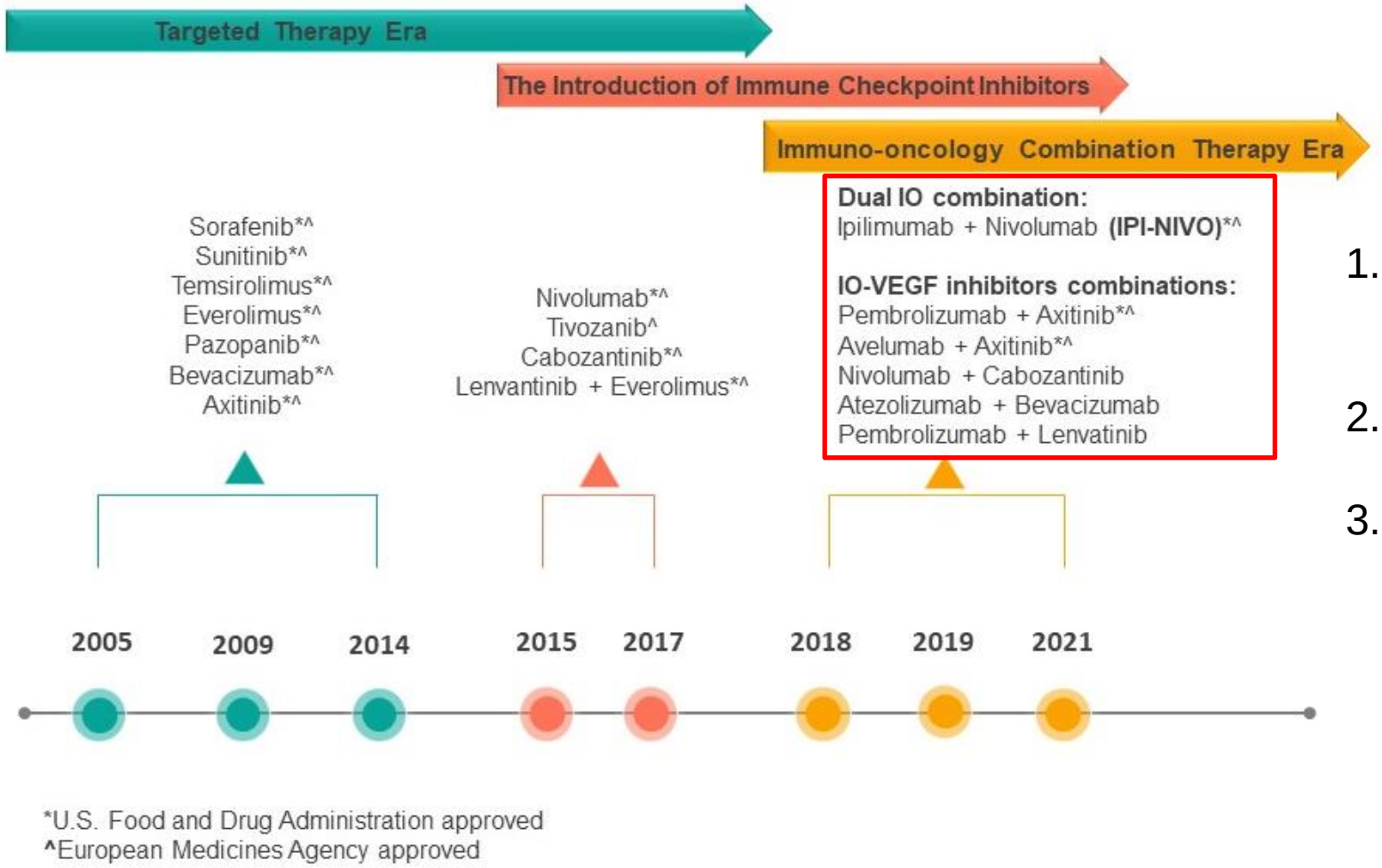
The Evolving Treatment Landscape in Metastatic Clear Cell RCC



Key Questions

1. IPI-NIVO vs. IO-VEGF, which strategy is better?
2. Any predictive factors?
3. Association between immune related AEs and clinical outcomes?

Methods

- IMDC
  - From 12296 patients, we identified 723 patients treated with 1L IO Combos from 40+ centers worldwide
- Comparison Groups
  - **IPI-NIVO vs. IO-VEGF** (Pembrolizumab + Axitinib, Avelumab + Axitinib, and Nivolumab + Cabozantinib)
  - IMDC intermediate and poor risk patients
- Primary Outcomes
  - Overall response rate, treatment duration (TD), time to next treatment (TTNT) and overall survival (OS)
  - TTNT is defined by the time from initiation of systemic therapy to subsequent therapy or death
  - Multivariable Cox regression analysis was performed to control for imbalances in IMDC risk factors
- Secondary Outcomes
  - OS by subgroups
  - Rates of serious immune related AEs*****
  - Outcomes of those with serious immune related AEs vs. those without

*****Serious immune related AEs is defined by the need for high-dose glucocorticoids (≥40mg of prednisone/day or equivalent) and/or treatment interruption

Baseline Characteristics

	IPI-NIVO (n=571)	IO-VEGF (n=152)	P value
IMDC risk groups			
Favorable	9% (46/500)	33% (46/138)	< 0.01
Intermediate	58% (290/500)	53% (73/138)	
Poor	33% (164/500)	14% (19/138)	
IMDC intermediate/poor risk group			
Number of patients	**454**	**92***	
Age, median (IQR)	64 (59-70)	61 (55-67)	0.14
Male	72% (328/454)	72% (66/92)	0.92
Non-clear cell histology	13% (47/361)	6% (5/80)	0.09
Liver metastases	21% (93/447)	15% (13/87)	0.21
Bone metastases	38% (168/448)	32% (28/88)	0.31
Brain metastases	8% (37/447)	2% (2/86)	0.05
Sarcomatoid features	25% (83/329)	18% (15/83)	0.17
Nephrectomy	59% (266/454)	75% (69/92)	< 0.01
IMDC risk factors			
KPS <80	19% (83/436)	11% (10/90)	0.07
Diagnosis to therapy <1yr	82% (371/454)	79% (73/92)	0.59
Calcium > ULN	19% (83/428)	13% (11/84)	0.17
Haemoglobin < LLN	63% (284/454)	46% (42/92)	< 0.01
Neutrophils > ULN	18% (79/450)	10% (9/91)	0.07
Platelets > ULN	23% (103/450)	20% (18/92)	0.48

*Pembrolizumab + Axitinib (N=49), Avelumab + Axitinib (N=36), Nivolumab + Cabozantinib (N=7)

All patients

IMDC intermediate/poor risk

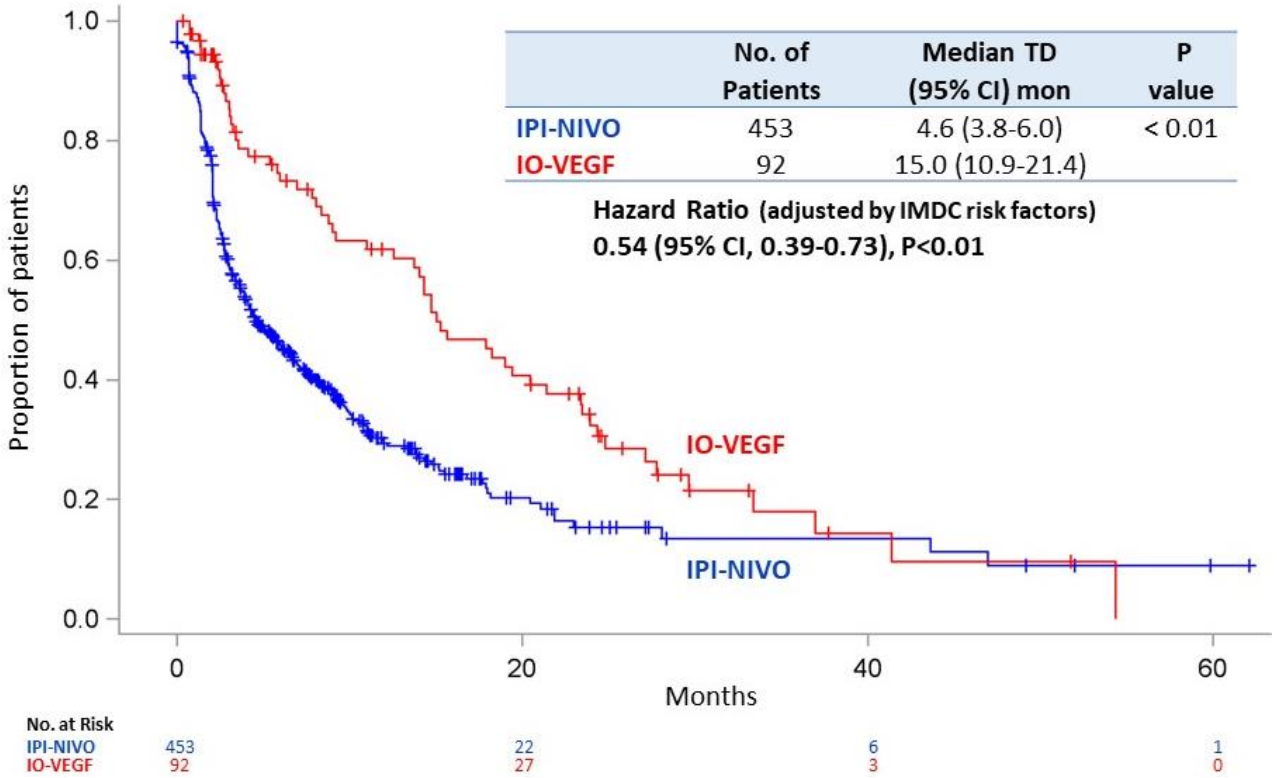
RESULTS

IMDC intermediate/poor risk

Overall response rate

Response rate	IPI-NIVO Mons (95% CI)	IO-VEGF Mons (95% CI)
ORR %, (n/n)	37 (143/382)	59 (43/73)
Best response %, (n/n)		
Complete response	4 (16/382)	4 (3/73)
Partial response	33 (127/382)	55 (40/73)
Stable disease	32 (120/382)	26 (19/73)
Progressive disease	31 (119/382)	15 (11//73)

Treatment Duration



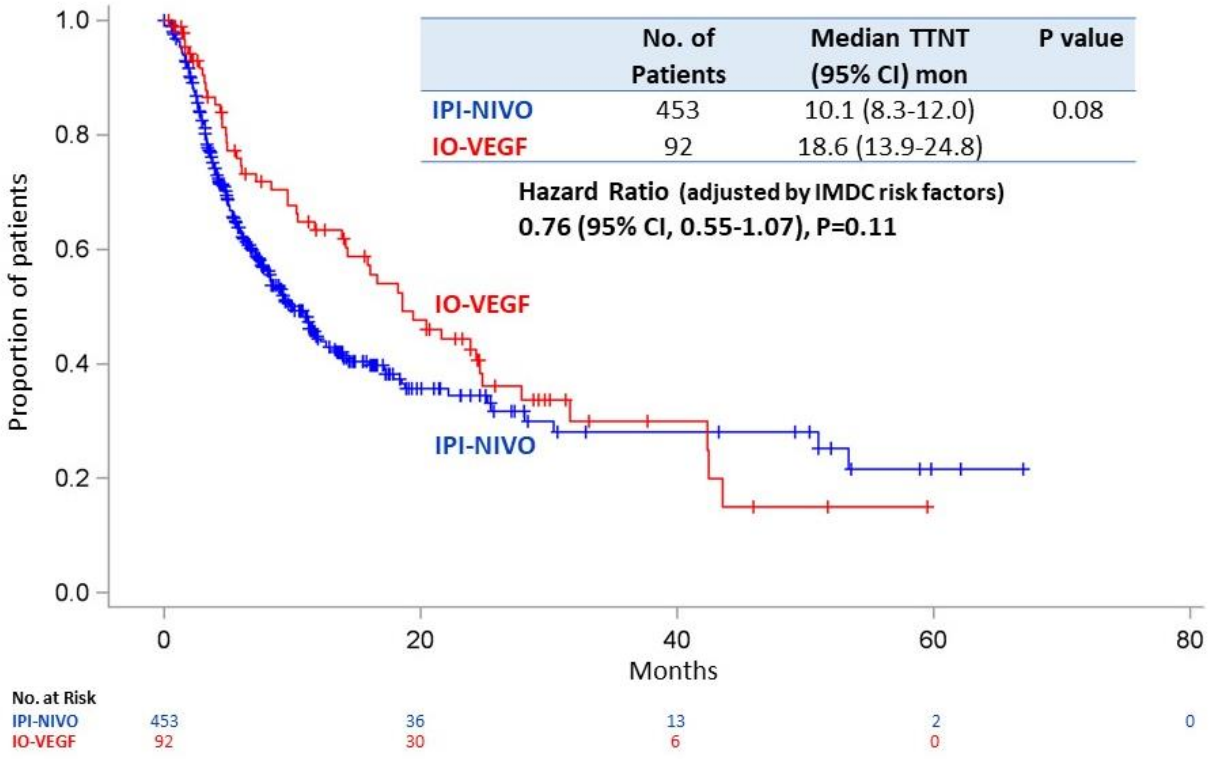
RESULTS

IMDC intermediate/poor risk

Time to Next Treatment

	No. of Patients	Median TTNT (95% CI) mon	P value
IPI-NIVO	453	10.1 (8.3-12.0)	0.08
IO-VEGF	92	18.6 (13.9-24.8)	

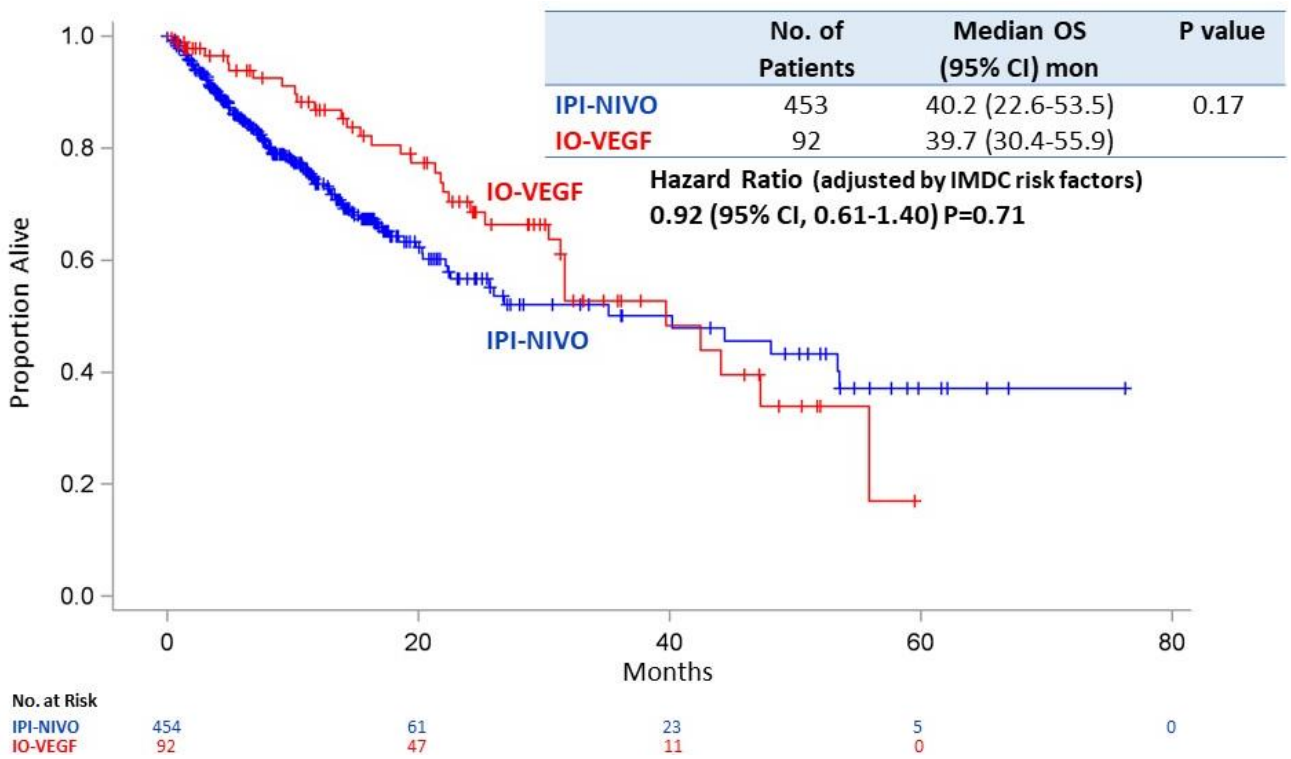
Hazard Ratio (adjusted by IMDC risk factors)
0.76 (95% CI, 0.55-1.07), P=0.11



Overall survival

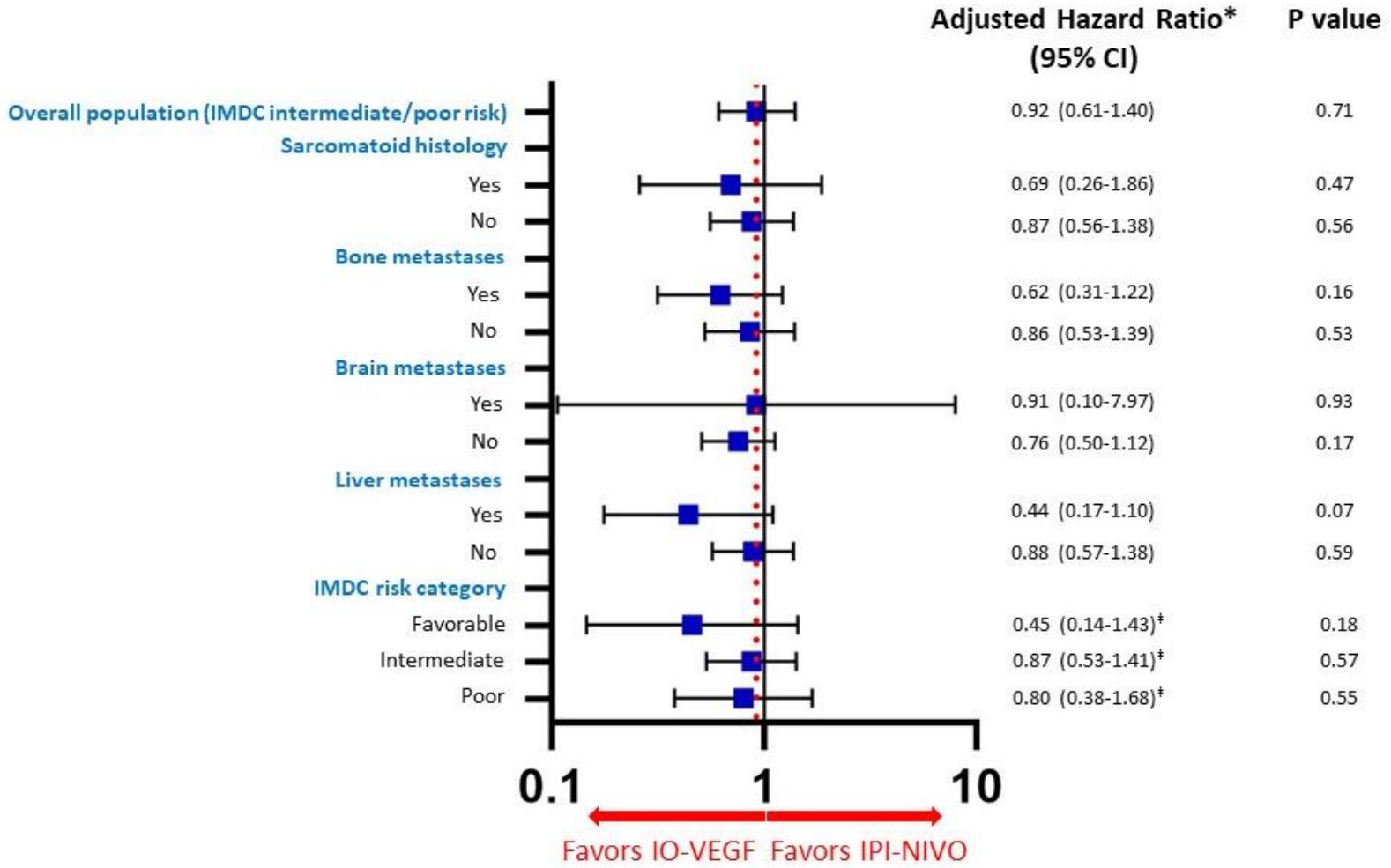
	No. of Patients	Median OS (95% CI) mon	P value
IPI-NIVO	453	40.2 (22.6-53.5)	0.17
IO-VEGF	92	39.7 (30.4-55.9)	

Hazard Ratio (adjusted by IMDC risk factors)
0.92 (95% CI, 0.61-1.40) P=0.71



No statistical difference between groups

Overall Survival by Subgroup†



†All subgroup analysis were performed on IMDC intermediate/poor risk patients, except IMDC risk category (which was performed on all IMDC risk patients)
*Adjusted by IMDC risk factors
‡ Univariate analysis

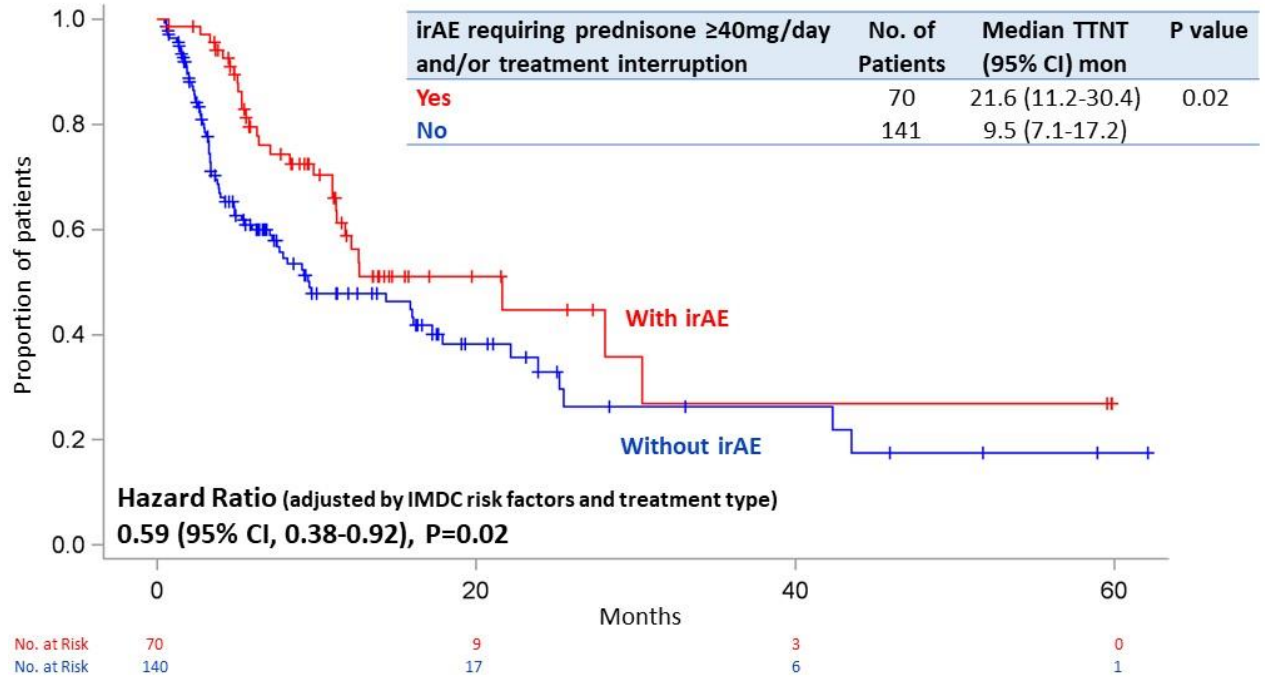
Rates of Serious Immune Related AEs by treatment

	IPI-NIVO % (N/N)	IO-VEGF % (N/N)	P Value
Serious Immune Related AEs*	37% (76/208)	13% (11/66)	<0.01

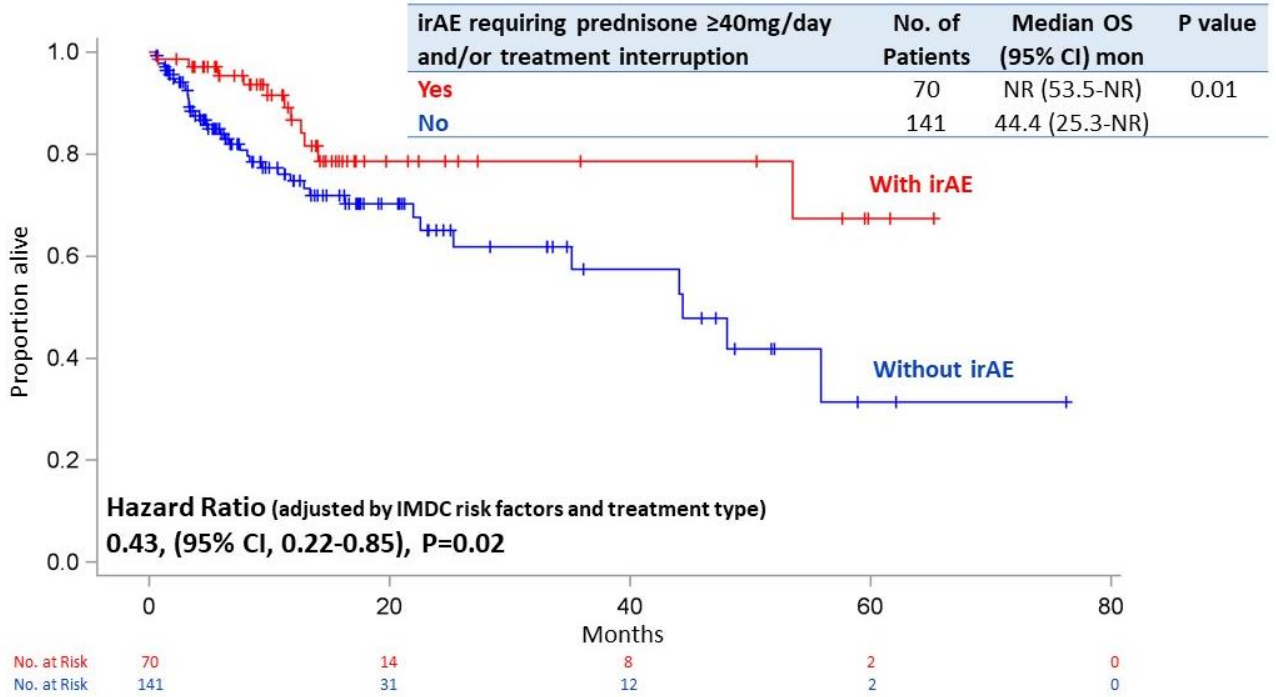
*Serious immune related AEs is defined by the need for high-dose glucocorticoids (≥40mg of prednisone/day or equivalent) and/or treatment interruption

Immune Related AEs and Outcome

Time to Next Treatment



Overall survival



No difference in treatment duration between the groups
irAE vs. Non-irAE: 8.9 (5.0-11.1) vs. 7.9 (5.5-12.6) months, p=0.78

Conclusions

- While there was a longer TD and higher ORR associated with IO-VEGF, **no differences** in TTNT and OS were detected between IPI-NIVO and IO-VEGF regimens in the IMDC intermediate/poor risk patients
- No clinical predictive factors were identified
- Serious immune-related AEs were associated with improved OS and TTNT
- Both IPI-NIVO and IO-VEGF are reasonable first-line strategies