Efficacy of immune-checkpoint inhibitors (ICIs) in the treatment of older adults with metastatic renal cell carcinoma (mRCC): An International mRCC Database Consortium (IMDC) analysis

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Background

- In metastatic renal-cell carcinoma (mRCC), inhibitors of the immune checkpoint programmed cell death protein-1 (PD-1) and its ligand (PD-L1), are now standard of care as either first-[1] or second-line[2] treatment.
- Despite not being excluded, older adults were underrepresented in registration trials of immune checkpoint inhibitors (ICIs).
- Given that immunological senescence may affect the anti-tumor activity of ICIs[3], there is uncertainty about the efficacy of ICIs in this population.
- Here we provide real world data on outcomes of older adults with mRCC treated with ICIs.

Methods

- Using the IMDC dataset, we identified all patients treated with a PD(L)1 ICI monotherapy or combination treatment in 1L, 2L or 3L between 2000-2019 and compared outcomes of older versus younger adults.
- Older adult was defined as ≥70-years at the time of ICI treatment initiation.
- Patients treated as part of a clinical trial were permitted for inclusion.
- Outcome measures of interest were: overall survival (OS); time to treatment failure (TTF); and response rate (RR)
- Summary statistics were calculated for all categorical variables. Multivariable Cox regression analysis was performed to control for imbalances in IMDC risk factors, line of therapy and histology.

Results

- 1427 patients with mRCC treated with PD(L)1 ICIs were included. Of those, 397 (28%) were older adults.
- **Table 1** summarizes demographic characteristics.
- **Table 2** summarizes outcomes of interest.
- RR between younger and older adults was significantly different (p = 0.01) and favored those <70 yrs. This was mainly driven by 1L results (p = 0.02)
- After adjustments, there was no difference in TTF and OS between younger and older adults.

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Abstract #5058

Table 1: Baseline Characteristics and IMDC Risk Factors

	Age < 70 (N = 1030)	Age ≥ 70 (N = 397)	P-value
Age, median (range)	60 (22-69)	74 (70-92)	**<0.01**
Male	761 (74%)	284 (71%)	0.34
ccRCC	859/985 (89%)	311/365 (85%)	**0.02**
Nephrectomy	841/1029 (82%)	313/396 (79%)	0.24
IMDC Risk Groups			0.55
Favorable	142/781 (18%)	46/299 (16%)	
Intermediate	462/781 (59%)	183/299 (61%)	
Poor	177/781 (23%)	70/299 (23%)	
Missing	249	98	
IMDC Risk Factors			
KPS < 80*	156/934 (17%)	74/365 (20%)	0.13
Diagnosis to therapy < 1 yr	604/1030 (58%)	204/397 (51%)	**0.01**
Calcium > ULN*	121/845 (14%)	41/330 (12%)	0.40
Hemoglobin < LLN*	526/946 (55%)	232/366 (63%)	**0.01**
Neutrophils > ULN*	89/922 (9%)	44/356 (12%)	0.15
Platelets > ULN*	123/943 (13%)	31/366 (8%)	**0.02**
Line of ICI			**<0.01**
1L	443/1030 (43%)	128/397 (32%)	
2L	478/1030 (46%)	215/397 (54%)	
3L	109 /1030 (11%)	54/397 (14%)	
1L ICI Treatments			
IO monotherapy	81/443 (18%)	27/128 (21%)	
IO-IO	193/443 (44%)	61/128 (48%)	0.35
IO-VEGF	169/443 (38%)	40/128 (31%)	

***At time of starting ICI therapy.** Abbreviations: KPS = Karnofsky performance status; LLN = Lower limit of normal; ccRCC = clear-cell renal-cell carcinoma; ULN = Upper limit of normal

Table 2: Outcomes of Interest

	Age < 70 (N = 1030)	Age ≥ 70 (N = 397)	P-value
Response Rate (%)	31	24	**0.01**
1L RR	44	31	**0.02**
2L-3L RR	20	20	0.86
Best Response			
CR	28/794 (3%)	2/278 (1%)	
PR	222/794 (28%)	64/278 (23%)	**< 0.01**
SD	259/794 (33%)	128/278 (46%)	
PD	285/794 (36%)	84/278 (30%)	
Time to Treatment Failure (months)	6.9 (5.7 – 8.3)	6.9 (5.5 – 8.4)	0.40
1L TTF	9.6 (7.8 – 11.8)	6.9 (4.96 – 9.3)	0.15
2L-3L TTF	5.0 (4.2 – 6.1)	6.9 (5.26 – 9.4)	0.66
Overall Survival (months)	30.9 (26.4 – 35.3)	25.0 (18.9 – 30.1)	**<0.01**
1L OS	41.4 (31.6 – 54.8)	28.5 (18.0 – 53.6)	0.01
2L-3L OS	25.9 (21.9 – 30.4)	23.8 (17.6 – 30.0)	0.34
Adjusted Hazard Ratios			
Time to Treatment Failure	0.95 (0.79 – 1.14)		0.59
Overall Survival	1.02 (0.79 – 1.30)		0.86

Abbreviations: RR = Response rate; TTF = Time to Treatment Failure; OS = Overall survival; CR = Complete response; PD = Progressive disease; PR = Partial response; SD = Stable disease

Figure 1: Overall Survival

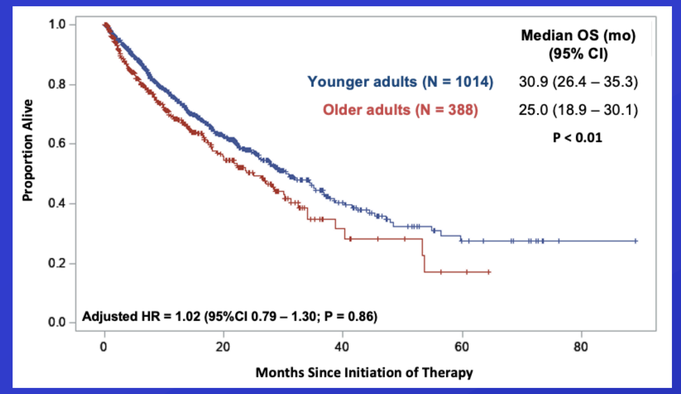
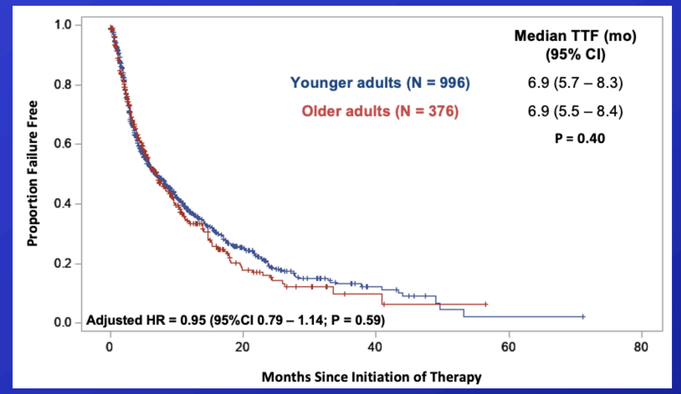


Figure 2: Time to Treatment Failure



Conclusions

- After multivariate adjustment, older adults with mRCC treated with ICI had no difference in OS and TTF compared to younger adults despite having a lower RR.
- Older age is not an independent risk factor for survival; thus treatment selection should not be based solely on chronological age.

References

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