Efficacy and Safety of First-Line Immune-Based Combinations in Metastatic Clear Cell Renal Cell Carcinoma in Older Patients

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Background

• Metastatic clear cell renal cell carcinoma (mccRCC) is mostly an elderly disease.
• First-line standard of care is based on immune-based combinations :
PD-1 inhibitor with VEGFR-TKI (= vascular endothelial growth factor inhibitors) or CTLA-4 inhibitor.
• Older patients (≥70 years) are underrepresented in pivotal phase III trials.
• Real-world data on efficacy and safety of these combinations in older patients are limited.

Methods

• Retrospective bicentric study (Tours University Hospital and CORT37)
• Inclusion of patients :
- With mccRCC.
- In first-line treatment with PD-1-based combination (ICI + VEGFR-TKI or dual ICI).
- Treatment initiated between Nov 2016 and Feb 2025.

Objectives

Primary objective:
• To compare overall survival (OS)
between patients aged ≥70 years and <70 years
treated with 1st line immune-based combinations for mccRCC.

Secondary objectives:
• Progression-free survival (PFS)
• Objective response rate (ORR) = Complete Response + Partial Response
• Safety profile

Results

Population characteristics

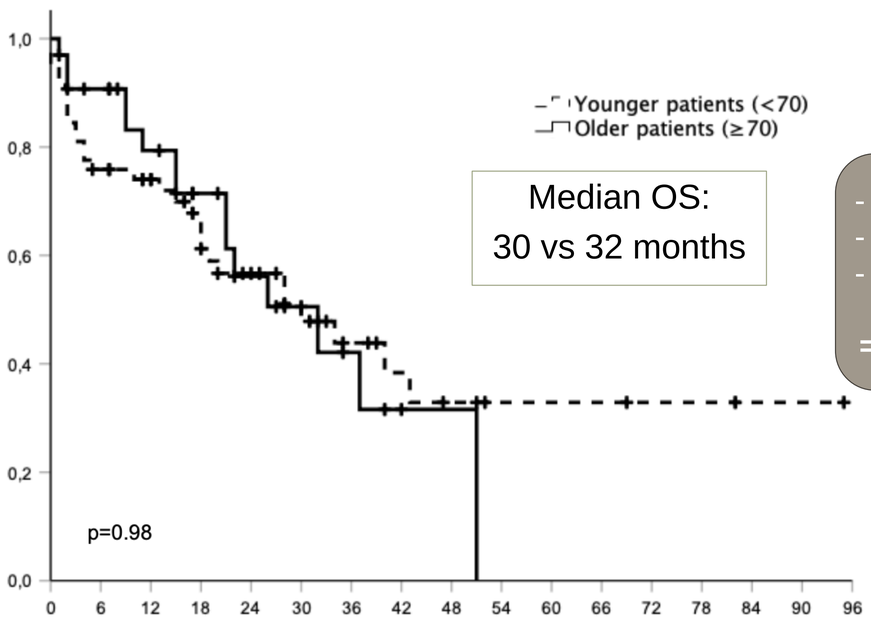
• N = 91 patients
– 33 (36%) aged ≥70 years
– 58 (64%) aged <70 years
• Median age: 64 years [29–86].
• Mostly men (78%), PS ECOG 0–1.
• **In the older group**:
more hypertension (82%) and malnutrition (6%),
but not polymedication (30%) ;
median Age Adjusted Charlson Comorbidity Index (aaCCI) = 4

Tumoral characteristics

	All patients n=91	Age <70 n=58	Age ≥70 n=33	P-value[1]
Metastatic at diagnosis	46 (51)	32 (55)	14 (42)	0.24
Metastatic sites				
Lung	68 (75)	39 (67)	29 (88)	**0.03**
Liver	26 (28)	18 (31)	8 (24)	0.49
Brain	8 (9)	4 (7)	4 (12)	0.47
Bone	25 (27)	17 (29)	8 (24)	0.60
IMDC risk groups				
Favorable	16 (18)	8 (14)	8 (24)	0.21
Intermediate	45 (49)	30 (52)	15 (45)	0.57
Poor	30 (33)	20 (34)	10 (30)	0.68
Nephrectomy	58 (64)	35 (60)	23 (70)	0.24
First line treatment				
Dual ICI: *Nivo/Ipi*	51 (56)	37 (64)	14 (42)	**0.05**
ICI + VEGFR-TKI :	40 (44)	21 (36)	19 (58)	
Nivo/Cabo	11 (12)	7 (12)	4 (12)	
Pembro/Axi	23 (25)	12 (21)	11 (33)	
Pembro/Lenva	6 (7)	2 (3)	4 (12)	

Values are in median [range] or number (pourcentage)
[1]P-values between the < 70 years old group and the ≥ 70 years old group

Primary objective: OS



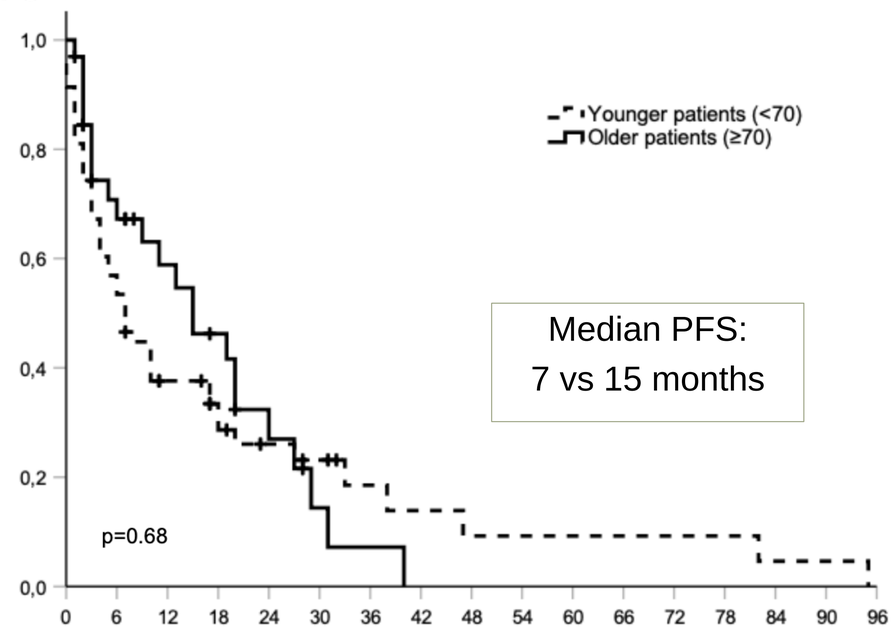
Median OS:
30 vs 32 months

- **Male**
- **BMI < 30 kg/m²**
- **Nephrectomy**

=> Reduced risk of death

Secondary objectives:

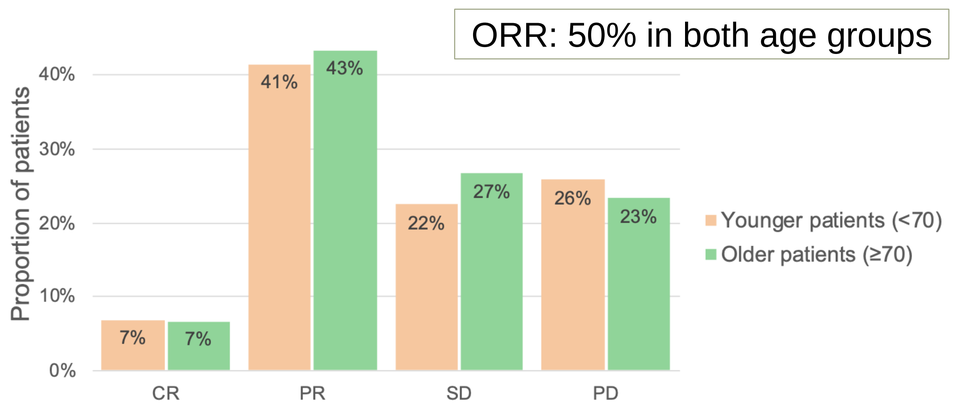
PFS



Median PFS:
7 vs 15 months

Tumor response

ORR: 50% in both age groups



Safety

No significant difference

• Any-grade treatment-related AEs: 81% in <70 years and 91% in ≥70 years
Grade 3–4 AEs: 38% in <70 years and 33% in ≥70 years
• Older patients: more gastrointestinal symptoms and hypertension.
• Younger patients: more hand–foot syndrome and cardiorespiratory events.
• Treatment discontinuation due to AEs: 14% (<70) vs 21% (≥70).

Conclusions & Perspectives

• With 91 patients, including 36% aged ≥70 years, this real-world bicentric study reports that:
– The ICI-TKI combinations were more frequently prescribed than the dual ICI in older patients.
– First-line immune-based combinations provide similar OS, PFS and ORR in older and younger patients.
– Safety profiles do not significantly differ between age groups in a selected older population.

Perspectives:
• Systematic geriatric assessment to better characterise frailty in older patients with mccRCC.
• Development of therapeutic drug monitoring for VEGFR-TKIs to account for pharmacokinetic variability and age-related changes.
• Further studies in even older patients (≥75 years) and less selected populations.

Clinical message:
Chronological age alone should not be a barrier to start 1st line immune-based combinations to fit older patients with metastatic clear cell RCC.