1461P - Impact of first-line (1L) therapy on outcomes of adult patients (pts) with metastatic MiT family translocation renal cell carcinomas (TRCC) treated in the contemporary immune checkpoint therapy (ICT) era

J.Thouvenin[1,2], O.Alhalabi[3], M.Carlo[4], L.Carril-Ajuria[5], Z.Bakouny[6], N.Martinez-Chanza[7], S.Négrier[8], L.Campedel[9], MA.Bilen[10], D.Borchiellini[11], J.Chahoud[12], Y-A.Vano[13], M.Lodi[1] P.Barthélémy[1], E.Hasanov[3], AW.Hahn[3], SR.Viswanathan[6], P.Msaouel[3], TK.Choueiri[6], L.Albiges[5], NM.Tannir[3*], GG.Malouf[1]

[1]Institut de Cancérologie Strasbourg Europe (ICANS), France; [2]Hospices Civils de Lyon, Pierre-Bénite, France; [3]MD Anderson Cancer Center (MDACC), USA; [4]Memorial Sloan Kettering Cancer Center, USA; [5]Institut Gustave Roussy, Villejuif, France; [6]Dana Farber Cancer Institute (DFCI), USA; [7]Institut Jules Bordet, Bruxelles, Belgium; [8]Centre Léon Bérard, Université Claude Bernard, Lyon, France; [9]AP-HP, Groupe hospitalier Pitié-Salpêtrière, France; [10]Winship Cancer Institute of Emory University, USA; [11]Antoine Lacassagne Cancer Center, Université Côte d'Azur, Nice, France; [12]Department of Genitourinary Oncology, Moffitt Cancer Center, USA.; [13]Department of Medical Oncology, Hôpital Européen Georges Pompidou, AP-HP, France.

BACKGROUND

- TRCC represent a rare and aggressive subgroup of RCC[1].
- While 1L therapy recommendations and clinical prognostication of pts with clear-cell RCC are well-known, data on TRCC clinical behavior are limited[1].
- TRCC is reported to be an immune cold tumor[3] and the data surrounding 1L ICT is scarce.

OBJECTIVES

To identify prognostic factors associated with 1L therapy in metastatic adult TRCC

To estimate overall survival (OS)

METHODS

- This is an international, multicenter retrospective cohort of metastatic adult TRCC patients treated in 1L across 11 genito-urinary oncology expert centers in France, Belgium and the US.
- Demographic and clinico-pathological data were recorded by investigators at each participating sites through a uniform de-identified database.
- Diagnosis of TRCC was confirmed by FISH.
- Patients were not selected on the basis of clinical factors and treatment were given to each center's standard of care.
- Univariable and multivariable analysis of prognostic factors on OS were performed.

RESULTS

BASELINE CHARACTERISTICS AND TREATMENT EXPOSURE (N=56)

Variable, n (%)	
Median age at diagnosis, years (range)	38 (16-62)
Sex - Male - Female	
Sites of metastatic disease[1] - Lymph nodes - Lung - Bone - Liver	 35 (62.5%) 31 (55.4%) 23 (41.1%) 21 (37.5%)
IMDC risk group - Favorable - Intermediate - Poor - NA[2]	 9 (16%) 38 (68%) 8 (14%) 1
De novo metastatic disease	29 (52%)
Previous nephrectomy	42 (75%)
Translocation type - TFE3 - TFEB	 47 (84%) 9 (16%)
1L therapies - VEGFR-TKI[3] - ICT combination[4] - Other regimens[5]	 32 (57.1%) 18 (32.2%) 6 (10.7%)

[1]Can be more than one site; [2]non available,[3]Tyrosine kinase inhibitor, [4]either combination of anti-PD-L1 and anti-CTLA-4 or ICT with VEGFR-TKI, [5]mostly chemotherapy or mTOR inhibitors

- **56 patients were included between December 2011 and December 2020**
- **At median follow-up of 27.8 months, 26 pts are still alive.**
- **Median OS is 13.5 months (mo) (95% CI: 3.9-NA) for pts treated with ICT compared with median 36.2 mo (95% CI: 27.7-NA) for pts who did not receive ICT in 1L; p=0.0014**
- **By multivariable analysis, 1L ICT and IMDC poor risk were the only variables associated with inferior survival (HR: 3.6; 95% CI (1.4-9.5); p=0.009 and HR: 4.6; 95%CI (1.05-19.9); p=0.04)**

Exploratory univariable analysis of prognostic factors on overall survival

Variables	Hazard ratio, (95%CI)	p-value
Sex (male vs female)	0.81 (0.39-1.7)	0.58
Age (sup or inf 37)	0.99 (0.48-2)	0.98
IMDC (poor vs intermediate/favorable)	4.2 (1.25-14)	0.02
Prior nephrectomy (yes vs no)	0.35 (0.16-0.78)	0.01
Type of translocation (TFEB vs TFE3)	2 (0.84-4.6)	0.12
Bone metastasis (yes vs no)	1.8 (0.88-3.7)	0.1
Brain metastasis (yes vs no)	1 (0.35-2.9)	1
Immunotherapy in first line treatment (yes vs no)	3.8 (1.6-8.9)	0.0025

Exploratory multivariable analysis of prognostic factors on overall survival

Variables	Hazard ratio, (95%CI)	p-value
Immunotherapy in first line treatment (yes vs no)	3.6 (1.4-9.5)	0.009
IMDC (poor vs intermediate/favorable)	4.6 (1.05-19.9)	0.04
Prior nephrectomy (yes vs no)	0.47 (0.1-1.4)	0.17
Bone metastasis (yes vs no)	0.96 (0.3-2.7)	0.94
Lung metastasis (yes vs no)	0.97 (0.4-2.5)	0.96

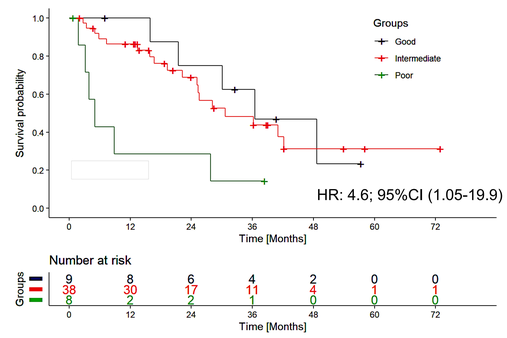

Figure 1: Kaplan-Meier curve for OS by IMDC risk group

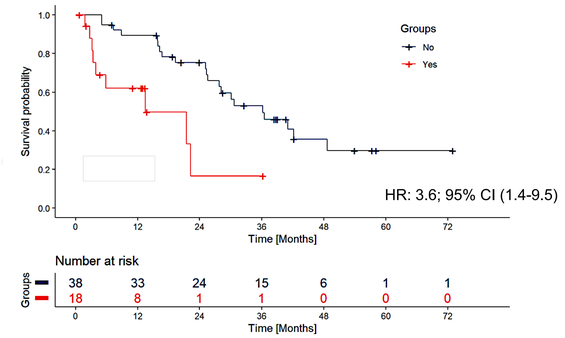

Figure 2: Kaplan-Meier curve for OS by 1L ICT

CONCLUSIONS

- **These data could suggest that some TRCC patients do not benefit of a 1L ICT and highlight the poorer prognosis and variability of this rare subtype of RCC compared to clear cell RCC.**
- **Further collaborative research efforts are needed to elucidate the biology underpinning these findings and to develop more effective therapies for TRCC.**

References:
[1]Simonaggio A et al. *Int J Mol Sci.* 2022
[2] Caliò A et al. *Cancers (Basel)*. 2019
[3]Sun G et al. *Nat Commun*. 2021

Correspondence: g.malouf@icans.eu