213P – Prognostic significance of absolute lymphocyte count in patients with metastatic renal cell carcinoma treated with first-line combination immunotherapies: Results from the International Metastatic Renal Cell Carcinoma Database Consortium (IMDC)

Kosuke Takemura[1*], Takeshi Yuasa[1], Audreylie Lemelin[2], Evan Ferrier[2], J. Connor Wells[3], Eddy Saad[4], Renee Maria Saliby[4], Naveen S. Basappa[5], Lori A. Wood[6], Evon Jude[7], Sumanta K. Pal[8], Frede Donskov[9,10], Benoit Beuselinck[11], Bernadett Szabados[12], Thomas Powles[12], Rana R. McKay[13], Georges Gebrael[14], Neeraj Agarwal[14], Toni K. Choueiri[4], Daniel Y.C. Heng[2]

[1]Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan; [2]Tom Baker Cancer Centre, University of Calgary, Calgary, AB, Canada; [3]BC Cancer Agency, Vancouver, BC, Canada; [4]Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, United States of America; [5]Cross Cancer Institute, University of Alberta, Edmonton, AB, Canada; [7]Queen Elizabeth II Health Sciences Centre, Dalhousie University, Halifax, NS, Canada; Olivia Newton-John Cancer Wellness & Research Centre, Heidelberg, VIC, Australia; [8]City of Hope Comprehensive Cancer Center, Duarte, CA, United States of America; [9]Aarhus University Hospital, Aarhus, Denmark; [10]University Hospital of Southern Denmark, Esbjerg, Denmark; [11]Leuven Cancer Institute, KU Leuven, Leuven, Belgium; [12]Barts Cancer Institute, Queen Mary University of London, London, United Kingdom; [13]Moores Cancer Center, University of California San Diego, La Jolla, CA, United States of America; [14]Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, United States of America

Background

- Lymphocytes are responsible for adaptive immunity and therefore are closely linked to mechanisms of action of immuno-oncology (IO) agents in patients with metastatic renal cell carcinoma (mRCC)
- We aimed to assess prognostic significance of absolute lymphocyte count (ALC) in a contemporary cohort of patients with mRCC

Methods

- Using the IMDC, data from patients with mRCC who received first-line IO-based regimens were analyzed (ie, nivolumab/ipilimumab, pembrolizumab/axitinib, avelumab/axitinib, nivolumab/cabozantinib, pembrolizumab/lenvatinib, and nivolumab/ipilimumab/cabozantinib)
- Baseline patient characteristics including best overall response per RECIST v1.1, time to next treatment (TTNT), and overall survival (OS) were compared with baseline lymphopenia (ie, ALC < 1000/μL)
- Descriptive statistics were compared using Fisher's exact tests or Mann–Whitney U tests. Kaplan–Meier curves were compared using log-rank tests. Hazard ratio (HR) and Harrell's C-index for prognostic factors were estimated using Cox proportional-hazards regression

Results

- A total of 195 (20%) of 966 patients had lymphopenia at baseline
- Brain metastases, bone metastases, and/or poorer best overall response were associated with presence of lymphopenia, whereas previous nephrectomy and/or the IMDC favourable-risk category were associated with absence of lymphopenia (**Table 1**)
- Patients with lymphopenia had shorter TTNT (10.1 vs. 24.3 months; $P < 0.001$) and OS (30.4 vs. 48.2 months; $P < 0.001$) (**Figure**)
- Lymphopenia was an independent adverse prognostic factor after adjustment for the IMDC risk factors (HR 1.68; $P < 0.001$) (**Table 2**)
- Incorporating lymphopenia into the IMDC criteria (ie, 6 factors vs. 7 factors) increased the C-index for OS prediction from 0.688 to 0.707

Conclusions

- Lymphopenia was a common laboratory abnormality that occurred in about one-fifth of previously untreated patients with mRCC
- Lymphopenia may serve as an indicator of poorer treatment response, shorter TTNT, and shorter OS in the contemporary IO era

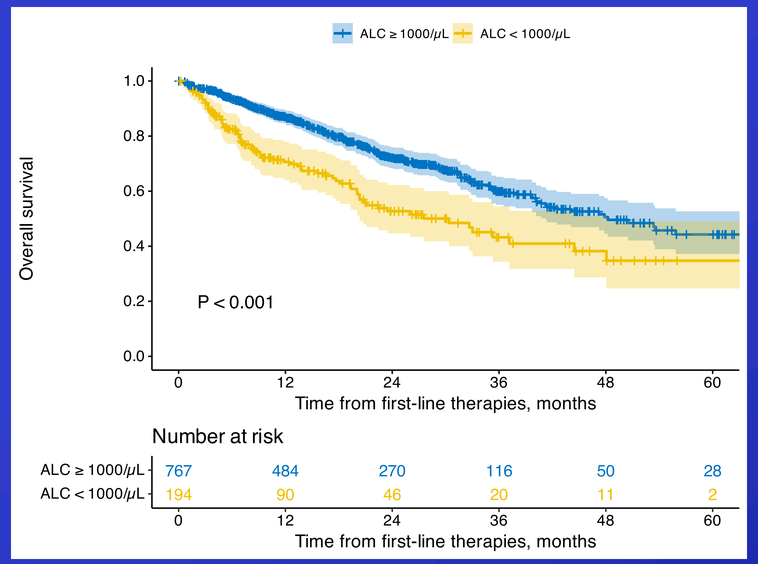

Figure. Kaplan–Meier curves for overall survival in patients with mRCC who did or did not have lymphopenia at initiation of systemic therapy

Table 1. Baseline patient characteristics

	ALC < 1000/μL (*N* = 195)		ALC ≥ 1000/μL (*N* = 771)		*P*
Age, median (IQR)	64 years	(56–71)	62 years	(56–69)	0.3
Male, *n* (%)	148/195	(76%)	565/771	(73%)	0.5
Previous nephrectomy, *n* (%)	99/193	(51%)	502/768	(65%)	< 0.001
Brain metastases, *n* (%)	21/185	(11%)	48/729	(6.6%)	0.041
Bone metastases, *n* (%)	102/189	(54%)	231/744	(31%)	< 0.001
Liver metastases, *n* (%)	30/185	(16%)	119/733	(16%)	> 0.9
IMDC risk, *n* (%)					0.012
Favourable	20/189	(11%)	142/728	(20%)	
Intermediate	110/189	(58%)	385/728	(53%)	
Poor	59/189	(31%)	201/728	(28%)	
Best overall response, *n* (%)					0.034
Complete response	4/163	(2.5%)	37/686	(5.4%)	
Partial response	56/163	(34%)	274/686	(40%)	
Stable disease	54/163	(33%)	235/686	(34%)	
Progressive disease	49/163	(30%)	140/686	(20%)	

Table 2. Multivariable analysis for OS

	HR	(95% CI)	*P*
Karnofsky performance status < 80%	2.35	(1.75–3.16)	< 0.001
Time from diagnosis to treatment < 1 year	1.57	(1.17–2.09)	0.003
Hemoglobin < LLN	1.26	(0.96–1.66)	0.099
Neutrophils > ULN	1.82	(1.30–2.54)	< 0.001
Lymphocytes < LLN	1.68	(1.27–2.23)	< 0.001
Platelets > ULN	1.01	(0.72–1.41)	> 0.9
Corrected calcium > ULN	1.13	(0.79–1.60)	0.5

LLN, lower limit of normal; ULN, upper limit of normal

*Correspondence to: Kosuke Takemura MD PhD MPH, Department of Genitourinary Oncology, Cancer Institute Hospital, Japanese Foundation for Cancer Research, 3-8-31 Ariake, Koto-ku, Tokyo 135-8550, JAPAN
kosuke.takemura@jfcr.or.jp @DrTakemura

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