310:Predictors of Objective Response to First-Line Immuno-Oncology Combination Therapies in Metastatic Renal Cell Carcinoma Results from the International Metastatic Renal Cell Carcinoma Database Consortium (IMDC)

Vishal Navani[1], Matthew Scott Ernst[1] , Connor Wells[2], Takeshi Yuasa[3], Kosuke Takemura[1], Frede Donskov[4], Naveen S Basappa[5] , Andrew Lachlan Schmidt[6] , Sumanta Pal[7], Luis Meza[7], Lori Wood[8], D Scott Ernst[9], Bernadett Szabados[10] , Rana R McKay[11], Andrew James Weickhardt[12], Cristina Suarez[13], Anil Kapoor[14], Jae-Lyun Lee[15], Toni K Chouieri[6], Daniel Y C Heng[1]

1 – Tom Baker Cancer Centre, Calgary, Canada 2 – BC Cancer Agency, Vancouver, Canada 3—Cancer Institute Hospital of Japanese Foundation of Cancer Research, Tokyo, Japan 4 – Aarhus University Hospital, Aarhus, Denmark 5 – Cross Cancer Institute, Edmonton, Canada 6 – Dana Faber Cancer Institute, Boston, USA States 7 – City of Hope Comprehensive Cancer Center, Duarte, United States 8 –Queen Elizabeth II Health Sciences Centre, Halifax, Canada 9 – London Regional Cancer Program, London, Canada 10 – Barts Cancer Institute, London, United Kingdom 11 -UCSD Moores Cancer Centre, La Jolla, USA 12 – Austin Health, Melbourne, Australia 13- Vall D'Hebron Institute of Oncology, Barcelona, Spain 14- Juravinski Cancer Centre, Hamilton, Canada 15– Asan Medical Centre, Seoul, South Korea

Background

The clinical impact of physician assessed real world imaging response to 1L IO combinations in metastatic Renal Cell Carcinoma (mRCC) remains uncharacterised. Underlying baseline characteristics associated with imaging response are lacking

Methods

IMDC database: Large Multi-centre International Cohort Study involving collaborators across 40 countries

1L Ipilimumab/Nivolumab (IOIO) or approved IO/vascular endothelial growth factor receptor inhibitors (IOVE)

Patients classified as per RECIST v1.1 as responders: complete responders (CR) or partial responders (PR) or non-responders: stable disease (SD) and progressive disease (PD)

Primary Outcome: Identification of baseline characteristics associated with real world physician assessed imaging response using adjusted logistic regression

Secondary Outcomes: Overall survival (OS) and time to next treatment (TTNT) based on physician assessed BOR

Results

Out of 1084 patients, 794 (73%) received IPI-NIVO and 290 (27%) received IOVE (axitinib+pembrolizumab, cabozantinib+nivolumab, axitinib+avelumab, lenvatinib+pembrolizumab). Favourable, intermediate and poor IMDC risk comprised 147 (16%), 517 (55%) and 272 (29%) respectively.

Of the 898 patients with evaluable responses, 37 (4%) achieved a best response of CR, 343 (38%) PR, 315 (35%) SD and 203 (23%) PD. Corresponding median overall survival from time of 1L initiation was: not reached, 55.9, 48.1, and 13 months respectively (logrank p < 0.0001).

In a multivariable model, lung metastases (Odds Ratio 1.71) and cytoreductive nephrectomy (OR 1.47) retained independent association with response, after adjustment for IMDC criteria. Factors not associated with response included (with univariable p values): gender (p = 0.58), age (p = 0.06), sarcomatoid histology (p = 0.99), smoking status (p = 0.92), liver (p = 0.62) and brain (p = 0.12) metastases. As in the VEGF monotherapy era, improved IMDC prognostic risk (OR 2.44) was associated with response.

Conclusions

- **Lung metastases (OR 1.71)**
- **Cytoreductive Nephrectomy (OR 1.47)**
- **Favourable IMDC Risk Group (OR 2.44)**

are independently associated with an increased odds of objective imaging response to 1L IO combination therapies

- Improved Imaging Response is associated with substantially longer OS and TTNT
- Patients can be counselled that if any of these baseline characteristics are present, there is an increased likelihood of experiencing tumour shrinkage to 1L IO combination therapies

Figure 1A: OS Kaplan Meier Curves by BOR

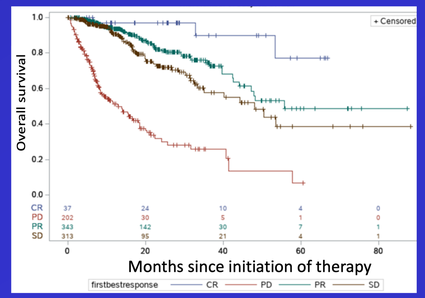

Figure 1B: OS Kaplan Meier Curves by Response vs No Response

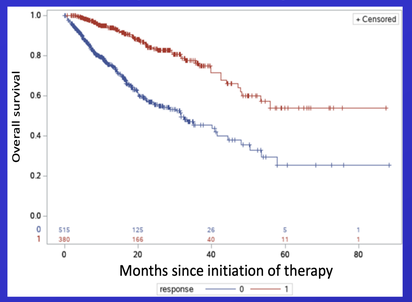

Figure 1A: TTNT Kaplan Meier Curves by BOR

Figure 2B: TTNT Kaplan Meier Curves by Response vs No Response

Table 1 Univariable and Multivariable Logistic Regression for associations between characteristics and objective imaging response

Baseline Characteristics		Univariable Analysis			Multivariable Analysis		
		Odds Ratio	95% CI	p Value	Odds Ratio	95% CI	p Value
Sex	Male vs Female	1.09	0.81-1.48	0.58			
Age	≥ 70 vs <70	0.74	0.53-1.02	0.060			
Smoking	Current vs Never	1.03	0.62-1.69	0.92			
Clear Cell	Clear Cell vs Non	1.71	1.07 – 2.71	0.024			
Sarcomatoid	Sacromatoid vs Non	1.00	0.68-1.46	0.995			
Cytoreductive Nephrectomy	**Yes vs No**	**1.57**	**1.13-2.19**	**0.007**	**1.47**	**1.02-2.10**	**0.038**
Lung Metastases	**Present vs Absent**	**1.71**	**1.26 – 2.31**	**<0.001**	**1.71**	**1.21-2.33**	**0.001**
Lymph Node Metastases	Present vs Absent	1.16	0.89-1.52	0.278			
Bone Mets	Present vs Absent	0.75	0.56-0.99	0.056			
Pancreatic Metastases	Present vs Absent	0.78	0.49-1.25	0.297			
Liver Metastases	Present vs Absent	0.91	0.63-1.32	0.628			
Brain Metastases	Present vs Absent	0.61	0.33-1.13	0.116			
IMDC Risk Group	**Favourable vs Poor**	**2.17**	**1.39-3.39**	**<0.001**	**2.44**	**1.53-3.82**	**<0.001**
IMDC Risk Group	**Intermediate vs Poor**	**1.53**	**1.10-2.13**	**0.010**	**1.61**	**1.13-2.24**	**0.006**
IMDC Risk Group	Favourable vs Intermediate	1.42	0.96-2.11	0.082			

Correspondence to: Daniel YC Heng MD MPH FRCPC, Tom Baker Cancer Centre, Calgary, Alberta, Canada. **Daniel.Heng@ahs.ca** **@DrDanielHeng**