Background: Non-clear cell RCC (nccRCC) represents a heterogenous group of tumors which is less well studied than clear cell RCC. Clinical data supporting the treatment of nccRCC are still based predominantly on clinical trials conducted in cRCC. There is very little known about this group of patients in Asia. In this study, we aim to report the real world outcomes of nccRCC patients in a cancer centre in Singapore.

Methods: We conducted a retrospective analysis on 99 non-clear cell RCC patients treated at the National Cancer Centre Singapore from 2009-2018. Data on patient demographics, disease characteristics, treatment outcomes and adverse events were collected retrospectively up till March 2020. Overall survival (OS) and progression free survival (PFS) were estimated using the Kaplan-Meier method. Responses to treatment were recorded based on RECIST v1.1 and analyzed using logistic regression.

Results: 99 patients were included in this analysis, with a median age at diagnosis of 56.7 years old. Papillary RCC accounted for 30.3% (n=30) of the cases, chromophobe RCC for 2% (n=2), unclassified RCC for 56.6% (n=56) and other subtypes for 11.1% (n=11). Median follow-up time was 24 months. Among this cohort, 72 patients (73%) received tyrosine kinase inhibitors (TKI), 14 patients (14%) had cytokine while 13 patients (13%) underwent other treatment. Median OS for the cohort was 13.4 months, while median PFS was 2.82 months. Overall response rate (CR+PR) for first-line treatment was 20.2%. In terms of safety outcomes, 29.3% of patients experienced severe adverse events (Grade 3 and above) while undergoing treatment. The most common adverse events severe reported were hand-foot syndrome (5.05%) and diarrhoea (4.04%).

Conclusions: This real-world study provides important data regarding clinical outcomes in this rare and heterogeneous group of renal cell carcinoma patients. There relatively modest survival outcomes reflect the need to better therapies for this patient group.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2020.10.213

Background: Non-clear cell renal cell carcinoma (nccRCC) represents a heterogenous group of RCC with limited representation in clinical trials due to their rarity and diverse histopathology. Thus, real-world data becomes important to give clue to the treating physicians for selecting the best possible treatment.

Methods: This is a retrospective, single center study to evaluate the outcomes of patients with nccRCC diagnosed and treated at Tata Memorial Center, Mumbai between 2017 and 2019. Baseline clinical features, histologic subtypes, therapeutic management and survival status were analyzed. SPPS version 20 was used for all statistical analyses.

Results: A total of 159 consecutive patients of nccRCC were evaluated for this study, 20 patients were excluded as these patients defaulted after their first visit. Out of 139 evaluable patients, 71.2% were males, the median age at diagnosis was 57 years (range: 10-81). Histologic subtypes comprised 76.2% papillary carcinoma, 6.5% sarcomatoid, 7.9% chromophobe, 1.4% unclassified tumors, and 0.7% oncocytoma. 51 (32%) patients were metastatic at presentation; 3 received supportive care alone due to poor performance status, 39.2% received sorafenib, sunitinib 27.4%, pazopanib 21.6% while bevacizumab erlotinib was given to 5.9% patients as first-line therapy. The median PFS of the overall patients was 6 months (95% CI: 2.4–9.6). The best response was partial response in 16.6%, stable disease 37.5%, and progressive disease in 45.8% of the patients. Only 23 (43.8%) could receive second-line therapy with everolimus being the most commonly used (38%). At the time of the data cut-off point (July 1, 2020), 29 metastatic patients had died, with a median overall survival of 11.9 months (95% CI: 5.4–18.4) with a median follow up of 14 months.

Conclusions: Papillary RCC comprised of the majority of the patients with nccRCC. This study reports worse survival outcomes as compared to other published studies. This might arise due to less use of subsequent lines of therapy and extremely low use of immunotherapy in the real-world scenario. Overall, the prognosis of nccRCC remains poor with a significant room for improvement.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2020.10.215

Background: VHL is one of the most commonly mutated oncogene in RCC. However, different co-mutated genes and VHL mutation types are associated with different prognoses and treatments. A more comprehensive understanding of the genomic landscape relative to different VHL variant subsets will help guide therapeutic development.

Methods: Molecular profiles of 322 RCC samples were obtained using next-genera- tion sequencing of 808 genes (Acornmed Corporation) and classified based on the presence and types of VHL variant. Incidence of VHL mutations was noted across the cohort. Co-occurring genomic alterations and tumor mutational burden (TMB) were analyzed.

Results: Across the entire cohort, 163 VHL mutations were detected among 154 patients(47.8%). Frameshift mutations were the most prevalent mutation type, accounting for the 42.9%(70/163), followed by missense, nonsense, splicing mutation, copy number loss(42.4%(69/163), 9.2%(15/163), 4.3%(7/163) and 1.2%(2/163) respectively). These mutations were classified into structural variant(58.4%) and non-structural variant(41.6%) based on the effects of variants on protein structure. PBRM1, SETD2, BAP1, KDM5C were commonly co-occurring with VHL(all p<0.05). SETD2 and KDM5C mutations were more common in VHL-nos RCC, followed by VHL-wt and the VHL-wt. BAP1 has a similar mutation frequency in cases of VHL-wt and VHL-nos, while VHL-wt had a lower frequency. PBRM1 was mutated in 10.1% of VHL wild type RCC but more frequently noted in both VHL subtype, with the higher rate in VHL-wt (43.3%) and lower in VHL-nos(29.7%). TMB-H was defined by >12.8 mutations/ Mb(upper quartile of the cohort). TMB-H varied across the different VHL mutation subset, most common in VHL-wt(31.1%) and least common in VHL wild type(VHL-wt) (22.2%).

Conclusions: VHL mutations are relatively common in Renal Cell Carcinoma and VHL structural variant is the most common type. The different VHL mutation has different co-occurring mutations and a different genomic landscape. VHL-wt was associated with the highest rate of TMB and PBRM1 frequency. These different clinical correlates in terms of therapeutic interventions need to be investigated.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.


https://doi.org/10.1016/j.annonc.2020.10.225

Background: PARACHUTE, a phase IV, observational study of treatment patterns and outcomes were recorded based on RECIST v1.1 and analyzed using logistic regression. The median PFS of the overall patients was 6 months (95% CI: 2.4–9.6). The best response was partial response in 16.6%, stable disease 37.5%, and progressive disease in 45.8% of the patients. Only 23(43.8%) could receive second-line therapy with everolimus being the most commonly used (38%). At the time of the data cut-off point (July 1, 2020), 29 metastatic patients had died, with a median overall survival of 11.9 months (95% CI: 5.4–18.4) with a median follow up of 14 months.

Conclusions: Papillary RCC comprised of the majority of the patients with nccRCC. This study reports worse survival outcomes as compared to other published studies. This might arise due to less use of subsequent lines of therapy and extremely low use of immunotherapy in the real-world scenario. Overall, the prognosis of nccRCC remains poor with a significant room for improvement.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2020.10.214