Currently 7 targeted therapies have been approved for the treatment of advanced RCC: sorafenib, sunitinib, temsirolimus, axitinib, bevacizumab in combination with interferon-α, everolimus and pazopanib (1). There is difficulty distinguishing between them due to lack of head to head studies. Therefore there are multiple treatment options for patients in the first and second line setting.

Due to clinical trial design, specifically cross-over and the influence of subsequent therapies, few of these drugs have proven overall survival benefit compared to the control arm (2,3). Despite this, the development of targeted therapy has increased survival in metastatic renal cancer approximately 2 fold (2,4).

There is huge variation in outcome to targeted therapy within the patient population. This is coupled with a lack of biomarkers to predict response and inadequate detail on the biological mechanisms of drug failure. Sophisticated imaging and biomarker analysis have not proved helpful in the identification of patients who might benefit from treatment (5). Therefore one could argue we have made very little progress in the drive towards personalized medicine and only identified new hurdles, such as tumour heterogeneity (6). Moreover evidence suggests that targeted therapy is associated with distinct molecular profiles which are of prognostic relevance. In this manuscript, the prognosis of the cytokine expression appears more significant than other prognostic models such as Heng prognostic scores and is therefore a step in the right direction. Unlike standard clinical classifications, however some plasma markers were also predictive of greater relative benefit from pazopanib.

For example patients with increased levels of cytokines especially interleukin 6 had a worse prognosis but a greater relative benefit from pazopanib. Although this study provides evidence that plasma markers can identify patients who receive greater relative benefit from pazopanib (as compared with placebo) it would indeed be interesting to see whether these marker would predict benefit from other treatment types e.g., mTOR inhibitors.
The findings from these studies support the approach of the use of cytokine and angiogenic factor (CAF) profiling to define biologically distinct subgroups of patients with metastatic renal cell carcinoma whose tumours have a greater angiogenic drive. CAF profiling might also be particularly well suited for angiogenesis inhibitors and other drugs targeting the tumour micro-environment, in which both circulating host derived and tumour derived factors could affect response.

Another possibility is to investigate dynamic changes to cytokines from sequential plasma, as this may better define a responding population. Finally, the integration of these prognostic and predictive factors with other significant factors such as single nucleotide polymorphisms may increase the power of these models (10). Powerful models predicting which patients benefit from specific agents is likely to be more useful than the development of further similar VEGF TKI therapies.

**Acknowledgements**

None.

**Footnote**

*Conflicts of Interest*: The authors have no conflicts of interest to declare.

**References**


