"Precision medicine" describes the integration of molecular profiling with clinico-pathological parameters to select optimal treatments for individual cancer patients. The majority of clear cell kidney cancers are highly VEGF dependent, due to inactivation of the von Hippel-Lindau tumour-suppressor gene which normally regulates vascular endothelial growth factor (VEGF) and platelet-derived growth factor (PDGF). Although current treatments for kidney cancer are biological agents targeting this commonly dysregulated pathway, no biomarker has been identified to select patients. Consequentially, small molecule inhibitors of VEGF and PDGF receptors, anti-VEGF-A monoclonal antibodies and mTOR inhibitors are used empirically in patients with advanced, progressing disease. New immune checkpoint inhibitors such as anti-programmed death 1 (PD1) antibodies have shown promise in clear cell kidney cancers, and tumour expression of PD1 ligand is a potential predictive biomarker which will be prospectively evaluated in ongoing phase III studies. In contrast to the relatively homogenous driver aberration in clear cell cancers, there is significant intratumoural heterogeneity which complicates rational drug design in this disease. Furthermore, marked clinical heterogeneity in the behaviour of kidney cancers already requires treating clinicians to individually tailor the timing of therapy based upon the pace of disease progression, permitting patients with relatively indolent cancers to undergo sometimes prolonged periods of monitoring whereas others will require rapid institution of systemic therapy. Again, this poses difficulties in designing and interpreting clinical trials. Classical clinical trial design using traditional endpoints may not always be the optimal method of evaluating new targeted agents, for which novel imaging techniques such as diffusion-weighted magnetic resonance imaging and positron emission tomography, or tumour biomarkers may be more appropriate. When traditional endpoints are selected, the integration of putative predictive biomarkers into trial design to enrich the patient population is vital to maximise the chance of detecting clinically useful new agents.

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