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Targeted therapies and the treatment of non-clear cell renal cell carcinoma

Table 1.
Clinicopathological features of the main RCC histological subtypes. Adapted from Lopez-Beltran et al. [2] and Atkins et al. [16]

RCC subtype	Incidence	Cell/tissue characteristics	Genetic features and characteristic hereditary alterations	Prognosis	Potential treatment
Clear cell	75%–90%	Clear cytoplasm, occasionally eosinophilic, hypervascular [17]	−3p, +5q22, −6q, −8p, −9p, −14q, *VHL* (3p25)	Aggressiveness according to grade, stage and sarcomatoid change	VEGF(R)- and mTOR-directed therapy
Papillary	10%–15%	Basophilic (type I) or eosinophilic (type II) cytoplasm, hypovascular [17, 18]	+3q, +7, +8, +12, +16, +17, +20, −Y, *c-MET* (type I), *Fumarate hydratase* (type II)	Aggressiveness according to grade, stage and sarcomatoid change	Activity reported with sunitinib, sorafenib, temsirolimus; possibly also everolimus and bevacizumab, MET-directed therapy (e.g. foretinib)? RET-directed therapy?
Chromophobe	4%–5%	Pale or eosinophilic granular cytoplasm, hypovascular [17, 18]	−1, −2, −6, −10, −13, −17, −21, hypodiploidy, *Birt–Hogg–Dube*	Tend to present with lower stage and grade than clear cell, with very low incidence of metastases. Overall prognosis may be no different to clear cell	Activity reported with sunitinib, sorafenib, temsirolimus, everolimus and pazopanib, KIT-directed therapy? RET-directed therapy?
Collecting ducts of Bellini	<1%	Eosinophilic cytoplasm, hypovascular [17, 19]	−1q, −6p, −8p, −13q, −21q, −3p (rare)	Aggressive: up to 40% of patients present with metastatic disease and a high proportion (~30%) have sarcomatoid features	Evidence to support the use of gemcitabine plus platinum-based therapy
Medullary	Rare	Eosinophilic cytoplasm, hypovascular [17, 20]	Rare loss of chromosome 22	Aggressive: mean survival of 15 weeks after diagnosis	
Xp11.2 translocation	Rare	Clear and eosinophilic cytoplasm, rich vasculature [21]	t(X;1)(p11.2;q21), t(X;17)(p11.2;q25), other	Some indolent, but aggressive particularly in adults	Activity reported with sunitinib, sorafenib and temsirolimus
Unclassified	4%–6%	Variable, sarcomatoid	Unknown	High mortality	For sarcomatoid: gemcitabine/doxorubicin; alternative: sunitinib ± gemcitabine, temsirolimus

mTOR, mammalian target of rapamycin; RCC, renal cell carcinoma; VEGFR, vascular endothelial growth factor receptor.

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