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KIDNEY CANCER

INHIBITION OF TK BETTER THAN MTOR

Patients with metastatic clear cell renal cell carcinoma (mccRCC) who are long-term responders to first-line tyrosine kinase inhibitors (TKIs) might benefit more from rechallenge with a TKI than switch to a mammalian target of rapamycin inhibitor (mTORI).

In a retrospective multicentre study, Reza Elaidi and colleagues reviewed the medical records of patients with mccRCC receiving sequential targeted therapy to determine whether, for second-line therapy, a TKI is preferable to an mTORI. Their analysis specifically focussed on individuals who had first-line TKI therapy for ≥6 months.

Of a total of 241 eligible patients, 85% had discontinued initial TKI therapy because of progressive disease, and the median first-line treatment duration (TD1) was 14.6 months (95% CI 12.8–17.2).

As second-line therapy, 118 patients had a TKI and 123 patients received an mTORI. Patient distribution was, overall, balanced, but more individuals in the mTORI group than in the TKI group were categorized as having poor prognosis (43% versus 27%). After a median follow-up period of 35.1 months and 22.9 months, respectively, 97 patients in the TKI group and 96 patients in the mTORI group had progressive disease.

In their analysis, the team used a Cox proportional-hazards regression model to estimate the relationship between the effect of treatment sequencing and end points (progression-free survival [PFS] or time to treatment failure [TTF]). Covariates included, for example, age at diagnosis, number of metastatic sites and TD1 (either as a continuous covariate or in fixed 6-month or 11-month intervals).

When considering TD1 as a continuous covariate, patients were found to benefit more from second-line TKIs than mTORIs (HR ≈ 0.75 for PFS and TTF). Notably, this finding was mainly due to the subgroup of patients who had received first-line TKIs for 11–22 months (median PFS 9.4 months versus 3.9 months for TKIs and mTORIs, respectively, $P = 0.003$, HR ≈ 0.5). Overall, analysis of the effect of second-line drug class and TD1 on PFS demonstrated that patients who had long-term second-line treatment responses were more likely to have been rechallenged with a TKI and to have had long-term first-line responses to a TKI.

Clemens Thoma

Original article Elaidi, R. *et al.* Outcomes from second-line therapy in long-term responders to first-line tyrosine kinase inhibitor in clear-cell metastatic renal cell carcinoma. *Ann. Oncol.* doi:10.1093/annonc/mdu552