Focusing on unknown clinical questions in mRCC

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mRCC Treatment goal in Europe and Japan
The treatment of metastatic renal cell carcinoma has changed significantly with the implementation of targeted therapies including drugs like sunitinib, sorafenib, temsirolimus, everolimus and pazopanib. Action of these drugs is based upon insights into the development of clear cell renal cell cancer involving the von Hippel-Lindau pathway and over expression of vascular endothelial growth factor (VEGF) and platelet derived growth factor (PDGF) as well as the involvement of the mTOR-pathway in the development and progression of kidney cancer. In Europe a treatment shift from cytokine therapy to therapy with target drugs has taken place. Above all with sunitinib an improvement in progression free survival and overall survival compared to interferon standard therapy has been shown in a prospective randomized trial. Interestingly in Japanese patients with metastatic renal cell cancer the median survival time is almost twice as long as the survival time in patients from Europe. In Japan cytokine therapy seems to be more widespread used than in Europe because for the therapy of metastatic renal cell cancer there. Also it seems that the treatment outcome regarding survival with cytokines has been better in Japanese patients compared to European patients. In part this might be due to a high rate of patients having received cytoreductive nephrectomy and metastasectomy. Possibly metastases are detected earlier because of very rigid follow-up schedules with regular CT scans. Aim of therapy however in both regions is prolongation of progression free survival and overall survival and preservation of an acceptable quality of life.

Prognostic predictive factors and factors for predicting effect - Differences between Europe and Japan -
Studies about predictive factors in metastatic renal cell cancer are mainly based upon cohorts from Northern America and Europe. The exclusion of Asian patients from these studies raises questions about the applicability of prognostic tools like the Motzer criteria. A large retrospective study about the prognosis of Japanese metastatic renal cell carcinoma patients treated in the cytokine era calculated a median overall survival of 21.4 months. This number is higher than survival rates published in European and Northern American studies (between 6 and 17 months). Multivariate analysis of these patients revealed the following independent prognostic factors: Time from initial visit to metastasis, ECOG performance status, lactate dehydrogenase, corrected serum calcium, and CRP. In contrast to the Motzer criteria, hemoglobin was not an independent prognostic factor.

When the strict Motzer criteria were applied to Japanese patients, even the median survival time in each prognostic group was longer than in the Motzer publication. However, the Motzer criteria clearly separated groups with different survival, although a subgroup of the poor prognostic patients with only three risk factors showed a relatively long survival.

In summary, prognostic factors have to be validated in Japanese patients although standard prognostic models yield acceptable predictions. Own comparative expression analysis on metastatic renal cell carcinoma patients revealed different endothelial markers such as CD31 or tetraspanin 7 as favourable prognostic markers. Future studies could aim at the comparison of such molecular predictors between patients from Asia and other ethnicities.

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