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Sunitinib

A Viewpoint by Michael Staehler

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Renal cell carcinoma (RCC) accounts for 3% of all adult malignancies, with about 200 000 cases per year worldwide and a rising incidence. As clinical symptoms are rare and often only present in later stages, up to 40% of patients have metastatic spread at initial diagnosis. The five year overall survival rate of all stages is only 62%. In metastatic disease (mRCC) this rate drops to approximately 5%. The only curative treatment is surgical removal of the primary tumour and the metastasis, if technically feasible. As chemotherapy and radiation therapy are ineffective, treatment of mRCC has so far been based on immunotherapy using interleukin-2 and/or interferon-α. Depending on regimen, response rates (including both partial and complete responses) vary from 5–30% in selected series. With such therapy, stable disease and prolongation of the time to progression are often the best achievable outcomes for patients with mRCC.

Sunitinib is an oral multikinase inhibitor of the angiogenetic pathway with substantial activity against the receptor tyrosine kinases vascular endothelial growth factor receptor, platelet-derived growth factor receptor and stem cell factor receptor. As a result, metastatic spread and tumour growth are effectively inhibited with this small molecule. In recent clinical trials, anti-tumour activity was demonstrated after failure of initial systemic therapy, mostly immunotherapy. In two multicentre phase II trials, a response rate of 39–40% was demonstrated with sunitinib treatment, and 23–28% of the recipients exhibited stable disease. The time to progression was prolonged to 8.7 months in comparison to approximately 5 months in historical controls. The latest data from an international multicentre phase III trial demonstrate a response rate of 37% with sunitinib compared to 9% in the control arm receiving low-dose interferon-α; 47% of suntinib recipients had stable disease.

Thus, sunitinib should be considered standard therapy in first line treatment of mRCC if combined immunotherapy is not feasible. The toxicity profile of sunitinib was demonstrated to be manageable, with fatigue, gastrointestinal and cardio-circulatory toxicities being the most common side effects. However, for about one third of the patients these side effects may be dose limiting. Our own experience shows that although oral administration is possible, the management of patients remains challenging especially with long-term therapy. Within the next few years, sunitinib will basically change the treatment of patients with inoperable mRCC with the addition of new treatment modalities based on this effective new drug. ▲