

Fact sheet 6 - New developments: Renal cell cancer

- **Targeted therapeutic agents**

Metastatic clear cell renal cell cancer has traditionally been treated with cytokines (interferon or interleukin-2). Improved understanding of biology has engendered novel targeted therapeutic agents that have altered the natural history of this disease. The vascular endothelial growth factor and its related receptor and the mTOR signal transduction pathway have particularly been exploited. Sunitinib malate, sorafenib tosylate, temsirolimus, and bevacizumab have improved clinical outcomes in randomized trials. Other multitargeted tyrosine kinase inhibitors (lapatinib, axitinib, pazopanib) and antiangiogenic agents (VEGF Trap, lenalidomide) have also demonstrated activity in early studies. Combinations of these agents are being evaluated.

The precise role of targeted agents in the treatment of metastatic disease and in adjuvant and neoadjuvant settings has yet to be defined. Drawing from their extensive experience of RCC, urologists will be instrumental in the design and application of clinical studies to define the role of targeted therapies in all settings of RCC and, ultimately, to integrate targeted therapies into clinical practice. The future of the therapy of renal cancer appears promising owing to the efficacy of these novel agents.

- **Biomarkers**

There is an obvious need to understand the genetics and molecular pathology of RCC to predict response to treatment and prognosis in individual patients. For example, the median survival for patients with metastatic disease is approximately 13 months. Therefore, there is a great need for biomarkers to predict metastasis and prognosis. In recent years, several promising biomarkers, including CAIX, B7-H1 and IMP3, have been identified by large retrospective studies. Further validation of these biomarkers is essential to transfer the research data into clinical practice. Eventually, an outcome prediction model with biomarkers, staging system and other risk factors will identify high-risk patients with likelihood of progression and formulate different follow-up protocols or systematic treatments for these patients.

- **Minimally invasive techniques**

The treatment of renal cell cancer (RCC) is rapidly evolving. During the last decade, an important trend towards minimally invasive treatment options has led to significant developments and procedures formerly considered experimental now being widely used for localised RCC. Laparoscopy has become an integral part of surgical treatments in many urologic departments worldwide. Laparoscopic or retroperitoneoscopic radical nephrectomy is an established procedure considered standard of care in Europe. Laparoscopic partial nephrectomy requires advanced surgical experience but is gaining increasing acceptance in the urologic community. For selected cases, thermal ablation techniques such as cryoablation and radiofrequency ablation are valuable therapeutic alternatives offering even less invasiveness and promising intermediate-term oncologic outcomes.

- **Vaccines**

Dendritic cell (DC) vaccines are an important experimental immunotherapy for renal cell carcinomas. To create the vaccine, cells will be removed from the patients tumor and fused with dendritic cells which are obtained from the patients blood. Dendritic cells are responsible for immune responses to "foreign" substances that enter the body. Animal studies have shown that these fused cells can stimulate powerful anti-tumor responses.

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DC vaccines have proven safe, but only minimal clinical efficacy has been observed to date. DC vaccine strategies reflect the continually evolving understanding of DC biology. The use of mature DCs is particularly important to avoid the induction of regulatory T cells. Better defined sources of immunizing antigens and more efficient antigen-loading will contribute to DC vaccines of better quality. Improved clinical efficacy may also be achieved using DCs that secrete biologically active IL-12, which fosters innate immunity and polarizes T helper type 1 responses that contribute to optimal antitumor immunity. Furthermore, combination therapies that treat systemic immune suppression will be crucial for obtaining improved clinical responses to DC vaccines in patients with advanced disease.