Surgical resection remains the cornerstone of treatment for kidney cancer. The cytokines interleukin-2 and interferon-alfa were, at one time, the only available approved systemic therapies for metastatic disease. However, the two agents are toxic when used in high doses and associated with clinical benefit for only a small subset of patients. The approval of targeted agents sunitinib, sorafenib, temsirolimus, and everolimus has offered the possibility of improved outcomes for a greater number of patients. This article reviews surgical options for metastatic renal cell carcinoma as well as clinical trial data on treatment strategies with cytokines and targeted agents.

Metastatic Renal Cell Carcinoma: Current Standards of Care

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Surgery is an important option for the initial treatment and palliation of symptoms from metastatic disease. Surgery remains the only curative option for nonmetastatic renal cell carcinoma (RCC). Radical nephrectomy, which includes a perifascial resection of the kidney, perirenal fat, regional lymph nodes, and ipsilateral adrenal gland, cures most patients with localized early-stage disease (Canda & Kirkali, 2006; National Comprehensive Cancer Network [NCCN], 2009). Radical nephrectomy is preferred for patients with large tumors or whose tumors extend into the inferior vena cava (Canda & Kirkali; NCCN).

Partial nephrectomy, or nephron-sparing surgery, preserves renal function. Because of advances in imaging techniques, tumors are being discovered at earlier stages. As a result, nephron-sparing surgery, which is recommended for tumors whose dimensions are 4–7 cm, is being increasingly used, producing outcomes equivalent to radical nephrectomy (Canda & Kirkali, 2006; NCCN, 2009). Patients with tumors in a peripheral location, or whose tumors are located over the upper or lower pole, are the most appropriate candidates for nephron-sparing surgery (NCCN), particularly important for patients who may already have had one kidney removed because of RCC or other reasons.

Surgical Management of Metastatic Renal Cell Carcinoma

About 25%–30% of patients with RCC present with metastases and about 20% of patients relapse even after complete resection of the primary tumor (Drucker, 2005; Schrader & Hofmann, 2008). An estimated 33%–50% of patients present with locally advanced or stage IV disease (Amato, 2005). The five-year survival rate for patients with metastatic RCC is less than 10% (Escudier, Eisen, et al., 2007). No systemic therapy used in the adjuvant setting has been proven to reduce the likelihood of relapse, which occurs most commonly in the lungs, bone, and brain (NCCN, 2009). For patients with metastatic RCC, surgical resection is used in combination with systemic therapy. Cytoreductive nephrectomy, by debulking the malignancy, can extend the survival of patients with metastatic disease. Randomized studies have shown that cytoreductive nephrectomy followed by systemic therapy can extend survival compared to systemic therapy alone (11.1 months versus 8.1 months; 17 months versus 7 months) (Flanigan et al., 2001; Mickisch, Garin, van Poppel, de Prijck, & Sylvester, 2001). Metastasectomy, or the surgical resection of metastases, also can be considered in some patients, particularly those with solitary or limited metastases (NCCN, 2009). In either of these settings, careful patient selection is