

The Value of Targeted Therapies in Kidney Cancer

Targeted therapies – drugs that inhibit or interfere with specific molecular pathways shown to be important in cancer cell growth – are providing clinicians with an armamentarium of therapeutic options for patients with advanced renal cell carcinoma (kidney cancer). They have already demonstrated their value with improved efficacy over interferon therapy based on results of randomized trials.¹ But, as clinical knowledge and experience in treating kidney cancer continues to advance, there is even greater potential for improving patient outcomes.

Key Stats

- Kidney cancer (excluding other and unspecified urinary organs) is the 14th most common cancer worldwide²
- According to the American Cancer Society, kidney cancer is among the 10 most common cancers in both men and women, with 15-25 percent of patients have mRCC where the cancer has spread to other parts of the body.³ Overall, the lifetime risk for developing kidney cancer is about 1 in 63 (1.6 percent), and the average age when diagnosed is 64⁴
- Most recent estimates for 2013 cite about 65,000 new cases of kidney cancer in the U.S., and about 14,000 deaths from this disease. (These statistics include both renal cell carcinomas and transitional cell carcinomas of the renal pelvis)⁴
- Kidney cancer is the eighth most common cancer in the UK (2010), accounting for around 3 percent of all new cases. In males, it is the seventh most common cancer (4 percent of the male total), while it is ninth in females (2 percent)⁵
- Most recent estimates of incidence of kidney cancer suggest that there are approximately 115,000 new cases each year in Europe, while approximately 49,000 people are likely to die from kidney cancer each year.²
- Renal cell carcinoma (RCC) accounts for approximately 85 to 95 percent of adult malignant kidney cancer cases⁶
- The rate of people developing kidney cancer has been rising steadily since the late 1990s. Yet the death rates for this cancer has gone down slightly since the middle of the 1990s⁴
- Overall, the estimated average five-year survival rates for patients with RCC are 96 percent for those presenting with stage I disease, 82 percent for those with stage II, 64 percent for stage III, and 23 percent for stage IV⁷

KEY TAKEAWAYS

Seven new medicines have been approved since 2005 for advanced kidney cancer

While the incidence rate of kidney cancer has been rising steadily since the late 1990s, death rates for this cancer has gone down since the middle of the 1990s⁴

Since around 2005, the median overall survival for patients with mRCC has increased from 10 to more than 20 months⁷

Background

For decades, cytokine therapy (e.g., interleukins and interferons) had been the standard of care in advanced or metastatic renal cell carcinoma (mRCC). And while cytokine therapy has produced complete remissions in 6 to 8 percent of patients, unfortunately, it is only appropriate for a small subset of patients who can tolerate it due to its toxicity profile.⁸ The variability in the clinical behavior of mRCC not only reflects the biological complexity of the disease, but it highlights the need for more effective treatments. Thanks to a greater understanding of the molecular biology of renal cell carcinoma in recent years (namely, the identification of signaling pathways), a number of newer agents (targeted therapies) are now available. These agents, while not devoid of their own toxicities, have provided more treatment options for a greater number of patients, and have begun to shift the treatment paradigms for advanced kidney disease.

The vast majority of kidney tumors are associated with an over-expression of a number of proteins such as vascular endothelial growth factor (VEGF) and platelet-derived growth factor (PDGF), which promote tumor growth.⁸ By inhibiting these signaling pathways, targeted therapies are thought to disrupt tumor growth, slow disease progression, and are intended to treat kidney cancer that has spread to other parts of the body. Because there are several pathways with an overlapping biologic function, having an agent (or agents) acting on multiple targets is an attractive option in mRCC.⁹

The heterogeneity of each patient, their ability to tolerate treatment, and the diversity in tumor characteristics has been and remains a key challenge to advancing clinical outcomes in mRCC. But having multiple targeted therapies available now provides physicians with choices that can increase the potential for helping more patients. In addition to their ability to inhibit specific pathways that tumor cells use to thrive, one targeted agent may offer advantages over another targeted agent, such as preferable pharmacodynamic or pharmacokinetic properties, an oral administration option, or a different side-effect profile. These are considerations that doctors and patients can and should make together when choosing the most appropriate treatment pathway. Just a decade ago, these treatment choices weren't available. Since around 2005, when targeted agents with activity against RCC began to appear, the median overall survival for patients with mRCC has increased from 10 months to more

than 20 months,⁷ so we are beginning to see progress. In the past decade, advances in research and drug development have begun to shift the treatment paradigm of this disease. And as the use of multiple targeted therapies in kidney cancer continues to be tested, we should see continued refinements of clinical practice guidelines.

Patient Perspective

Before his diagnosis, Chuck was busy working, raising children, and teaching Sunday school to people of all ages. Then he received the shocking news from his doctor that he had advanced kidney cancer. And while it took some time to come to terms with the diagnosis, he's had success controlling his cancer with the available treatments. (Note that the treatment success of one patient is not typical of most patients).

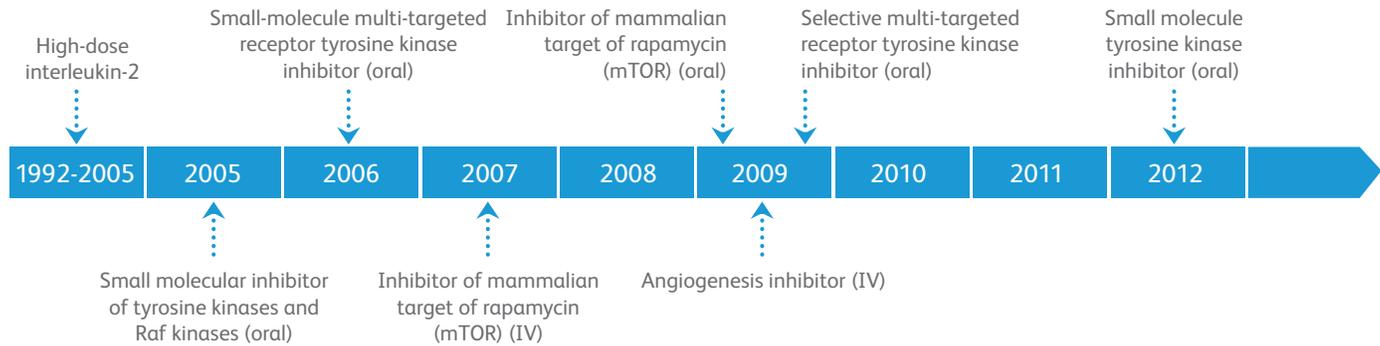
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“The diagnosis of kidney cancer was stunning. Fortunately, we were led to a great oncologist. He and his staff have taken outstanding care of me and Joan, and have been informative at every turn. I was delighted the doctor outlined treatment options and left the final decisions to us.”

– Chuck Hudson

The table below shows FDA approvals for advanced kidney cancer treatments over the past 3 decades.

HISTORY OF DEVELOPMENT: Targeted Treatment Options for Advanced RCC



Endnotes

- 1 Rodolfo Passalacqua, et al. Immunotherapy options in metastatic renal cell cancer: where we are and where we are going. *Expert Rev. Anticancer Ther.* (2006) 6(10), 1459-1472.
- 2 Globalcan 2012: Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2012. Retrieved from http://globocan.iarc.fr/Pages/fact_sheets_population.aspx
- 3 Kidney Cancer Association. Retrieved from <http://www.kidneycancer.org/knowledge/learn/about-kidney-cancer/>
- 4 American Cancer Society. Kidney Cancer Detailed Guide. Last Medical Review: 11/8/2012. Retrieved from <http://www.cancer.org/cancer/kidneycancer/detailedguide/kidney-cancer-adult-key-statistics>
- 5 Cancer Research UK. (Nov. 2013) Retrieved from <http://www.cancerresearchuk.org/cancer-info/cancerstats/types/kidney/incidence/>
- 6 Momoe Itsumi and Katsunori Tatsugami. Immunotherapy for Renal Cell Carcinoma, (2010), *Clinical and Developmental Immunology*. Volume 2010, Article ID 284581. doi:10.1155/2010/284581. Retrieved from <http://www.hindawi.com/journals/cdi/2010/284581/>
- 7 N. Chittoria, B. Rini. Renal Cell Carcinoma. Cleveland Clinic; Center for Continuing Education. (2013). Retrieved from <http://www.clevelandclinicmeded.com/medicalpubs/diseasemanagement/nephrology/renal-cell-carcinoma/#top>
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- 9 S. Oudard, D. George, J. Medioni, R. Motzer. Treatment options in renal cell carcinoma: past, present and future. *Annals of Oncology* Vol. 18 (Supplement 10): x25-x31. September 2007.

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