Renal Cell Carcinoma: The Fastest Evolving Tumor


Renal cell carcinoma (RCC) has been considered one of the most difficult tumors to treat for about 20 years. Chemotherapy and radiotherapy have almost no efficacy in this tumor, and cytokines (interleukin [IL]-2 [Proleukin] and interferon) have remained the only available treatment for about 20 years, with a small proportion of patients benefiting from these treatments.

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In 2007, four targeted therapies—sorafenib (Nexavar), sunitinib (Sutent), temsirolimus (Torisel), and bevacizumab (Avastin)—were shown to be active in large phase III trials,[1-4] leading to approval of these drugs by the US Food and Drug Administration (FDA) and the European Medicines Agency (EMEA). [Bevacizumab in combination with interferon has been approved by the EMEA but not yet by the FDA.] In addition, several other targeted agents are currently being investigated in phase III studies, and should be approved in the near future (eg, everolimus [Certican], which was recently reported to be active in tyrosine kinase inhibitor-refractory patients).[5]

Challenges for the Future

In their excellent review, Rini and Bukowski give a complete overview of these different drugs. Nevertheless, the challenges for the future of RCC therapy remain important, and the following issues still need to be addressed:

(1) Despite the efficacy of many drugs, the rate of complete remission in RCC patients remains extremely low. Whether a combination of active agents will allow an increase in complete remission rates is questionable.

(2) As additional drugs become available, sequential therapies with these agents are currently considered the standard of care. However, the best way to use these sequences is still empirical, and the mechanisms of resistance remain unknown.

(3) The use of these drugs in an adjuvant setting needs to be tested. Nevertheless, there is no evidence that the ongoing adjuvant trials will be positive, and one should be very careful when using such drugs in nonmetastatic RCC outside of clinical trials.

(4) Each of the currently approved drugs shows some specificity, which is still difficult to understand. As examples, we should determine in the future, why:

• Temsirolimus is more active in poor-risk patients than in good-risk individuals.
• Sorafenib appears to have little activity in the first-line setting compared to its activity in cytokine-refractory patients.
• Bevacizumab has shown promising activity in combination with interferon. Is the use of interferon (which adds toxicity) necessary for this activity?

Thus, although RCC appears to be easier to treat in 2008, the need for clinical trials is probably greater than ever, to get answers to the critical question for RCC patients: Will we someday be able to cure metastatic RCC?

Disclosures: Financial Disclosure: Dr. Escudier has received honoraria from Roche, Bayer, Novartis, and Wyeth Pharmaceuticals.

References:

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