

Case Based Urology Learning Program

Resident's Corner: *UROLOGY*

Case Number 9

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A 52-year-old healthy man is diagnosed with a 10.5 cm R renal mass with a level 2 IVC thrombus. He also is found to have 4-5 1-2 cm lung nodules highly suspicious for metastatic disease. There is no retroperitoneal lymphadenopathy and the metastatic evaluation is otherwise negative. The other kidney appears to be normal. PMHx includes HTN. The SCr level is 1.0 and eGFR is > 60.

What laboratory tests are particularly pertinent in this patient?

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Calcium, hemoglobin, and LDH. The main prognostic factors for patients with metastatic RCC (Motzer criteria) include metastasis free interval (< 1 year), suboptimal performance status, hypercalcemia, anemia, and elevated LDH. Other analyses have also added multiple sites of disease (3 or more sites) as an additional poor prognostic factor. Patients with none of these factors have good risk disease, those with 1 or 2 have intermediate risk disease, and those with 3 or more have poor risk disease. These risk categories have correlated with progression free survival in phase 3 clinical trials.

All laboratory tests are normal and performance status is excellent. The patient thus has intermediate risk disease, because the metastasis free interval is < 1 year due to synchronous presentation.

Should this patient be considered for cytoreductive nephrectomy, and what benefit can be expected in this setting?

Should this patient be considered for cytoreductive nephrectomy, and what benefit can be expected in this setting?

This patient is a good candidate for cytoreductive nephrectomy because he has good performance status and lung only metastasis, both of which have correlated with good outcomes from cytoreductive surgery. In general, cytoreduction will tend to extend survival about 40-50%, although it is not curative. For instance, if the patient was destined to live for 12 months with systemic therapy alone, one might anticipate about 18 month survival if cytoreductive nephrectomy was incorporated into the treatment paradigm. The other main factors to consider in deciding about cytoreductive surgery are that the main burden of disease should be in the involved kidney or adjacent retroperitoneum (otherwise substantial debulking will not be accomplished), cardiac and pulmonary status must be adequate to support major surgery, and for the most part patients with CNS and liver metastases have been excluded because they have such a poor prognosis.

Is this patient a candidate for
neoadjuvant targeted molecular
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Neoadjuvant therapy is still experimental and in general should be performed in a clinical trial setting to advance the field. This patient has no compelling reason for neoadjuvant therapy such as need to downsize the tumor to facilitate surgery, etc. Such patients are in reality uncommon. Anti-VEGF therapy can inhibit wound healing and the natural regeneration of the vasculature, and thus could potentially affect tissue and vascular integrity. Hence, such treatments are not risk free and the side effects can be substantial. This patient would not be a good candidate for neoadjuvant systemic therapy outside of a clinical/translational research trial.

The patient undergoes R radical nephrectomy and IVC thrombectomy and recovers uneventfully. Pathology is pT3b clear cell RCC, with negative margins and negative nodes. Recovery is uneventful.

What systemic therapy would be offered to this patient who is highly motivated for cure?

What systemic therapy would be offered to this patient who is highly motivated for cure?

High dose IL-2 is still the only systemic treatment for RCC that provides a reasonable possibility of cure. Complete remission rates of approximately 3-5% have been reported and can be durable. Other main options for this systemic treatment naïve patient with intermediate risk RCC include sunitinib or bevacizumab/IFN combination therapy.

What are the main side effects of high dose IL-2?

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High dose IL-2 can lead to a vascular leak syndrome that be associated with hypotension, oliguria, ARDS and other forms of organ failure. Severe side effects can be avoided in most healthy patients with careful medical care, but older or frail patients are very high risk for such complications and are generally excluded from this protocol.

What are the mechanisms of action of sunitinib and bevacizumab?

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Sunitinib is a tyrosine kinase inhibitor (TKI) that inhibits the receptor for VEGF and several other related receptors. Bevacizumab binds and sequesters VEGF and thus inhibits angiogenesis and other related pathways.

What are the main benefits and side effects of VEGF targeted molecular therapy?

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Several phase III clinical trials now demonstrate better progression free survival with these agents, and most are thought to also extend overall survival. Cross over within the clinical trials has made it difficult to establish an overall survival benefit in some trials but most trials suggest a survival benefit associated with these agents. In general, the side effects of these agents include cardiovascular (e.g. HTN), dermatologic (e.g. hand foot syndrome), GI, and constitutional (e.g. fatigue).

What other molecular pathway is commonly targeted in patients with metastatic RCC?

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The mTOR pathway is also a commonly targeted pathway in this disease, with agents such as temsirolimus and everolimus demonstrating activity against this malignancy.

What is the current algorithm for deciding which systemic therapy to use in individual patients with metastatic RCC?

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See selected reading for this as of 2010-2011.

Selected Reading

Rini BI: Metastatic RCC: Many treatment options, one patient. *J Clin Onc* 2009;27(19)3225-34.

Topic:

Oncology: Renal Tumors

Subtopics:

Metastatic Disease

Cytoreductive Nephrectomy