GENITOURINARY CANCERS INTERNATIONAL

International mRCC Database Consortium Seeks to Inform Prognosis, Prediction

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The field of metastatic renal cell carcinoma (mRCC) has experienced a therapeutic windfall in recent years with the approval of five VEGF inhibitors and two mTOR inhibitors, with many other investigational agents coming down the pike. And yet, clinicians may now be stymied by too much of a good thing because it is not readily apparent how best to use all these therapies in sequence.

As Daniel Heng, MD, MPH, of the Tom Baker Cancer Center at the University of Calgary, explained during the General Session on Renal Cancer—Genomics, Prognosis, and Therapies, the International mRCC Database Consortium (IMDC) can help make sense of the targeted therapy muddle. Currently featuring 3,537 patients with mRCC from 25 institutions around the world, the goals of the consortium are to harness the wealth of information being collected to identify trends in the use of targeted therapies in real-world practice, answer important clinical questions, and generate hypotheses ahead of clinical trials. Dr. Heng detailed how the IMDC data have been exploited thus far and where it is headed in the future.

Prognosis

IMDC researchers have developed a model using the data that stratifies patients by risk to gauge patient prognosis in the age of targeted therapy. The IMDC criteria assign one point to each of six adverse clinical factors—Karnofsky performance status less than 80%, an interval less than 1 year between diagnosis and treatment, anemia, thrombocytopenia, neutrophilia, and hypercalcemia—to sort patients with mRCC into favorable risk (zero factors), intermediate risk (one to two factors), and poor

medical, and radiation specialists from around the world congregated to exchange ideas, best practices, and scientific research that will lead to future progress in GU cancers. **Full Story**

Dr. Primo Lara Presents His Top Five Lists in Renal Cancer Research

Primo Lara, MD, of the UC Davis Comprehensive Cancer Center, counts down the top five successes and disappointments in the past 20 years of renal cancer research. High on the list of successes: multispecialty coordination in renal cancer research and patient care. **Full Story**

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In an attempt to make sense of the recent influx of treatments for metastatic renal cell carcinoma, the risk (three to six factors) groups. The model does an outstanding job of discriminating survival differences among the three groups, as demonstrated by median overall survival durations of 43.2 months, 22.5 months, and 7.8 months, respectively. Moreover, the IMDC criteria have been externally validated and prove to be more accurate compared with other prognostic models such as the Memorial Sloan Kettering Cancer Center model.

"There are much more complicated prognostic models and nomograms that you can put in your pocket, but they are difficult to remember. And if they are difficult to remember for a clinician like me, [and] they are hard to apply in the clinic," Dr. Heng said, further underscoring the benefit of the IMDC criteria.

Although Dr. Heng recognized that many other prognostic factors in mRCC exist, such as non–clear cell histology, prior nephrectomy, and liver and bone metastases, he noted that the addition of these other features to the IMDC criteria does not meaningfully improve discriminatory ability. "In the next jump for prognosis, we really require individualized tumor-specific tissue markers to make the next big step"—things like data on microRNA, biometrics, genomics, and single nucleotide polymorphisms, he said.

Dr. Heng also noted that more attention should be paid to conditional survival. "Prognostication should be dynamic," he said, meaning that prognostic criteria applied at the initiation of treatment may no longer apply after a patient survives beyond a particular point in time. Indeed, researchers analyzing IMDC data have found that as patients with poor risk live longer, their chances of surviving beyond 2 years begin to climb, even eclipsing that of patients with intermediate risk.

Prediction

Predictive markers prove essential in disease treatment to try to predetermine the efficacy and toxicity of treatment for a given patient. Whereas other cancers benefit from a range of biomarkers that predict the potential benefit of specific therapies, RCC has no such validated, reproducible markers as of yet.

In the absence of predictive markers, it remains unclear whether the order of consecutive targeted therapies makes a difference in mRCC. As Dr. Heng noted, the data available thus far beg the question of whether the sequence matters or whether the most important point is that patients have access to all available drugs, similar to the situation in non–small cell lung cancer.

Certain toxicity signals, such as hypertension, hand-foot syndrome, and fatigue, do show a correlation with survival outcomes in mRCC. However, these signals are not robust enough to warrant the cessation of therapy in the absence of side effects. Moreover, toxicity provides little insight into which drug to select for treatment because the signals do not arise until after treatment initiation.

To overcome the dearth of predictive markers, Dr. Heng believes that biomarkers are key to unlocking predictive ability in mRCC—markers such as MET, PDL-1, and PBRM1/BAP1. With support from the Kidney Cancer Association, the IMDC is laying the groundwork for mass biomarker discovery by collecting tissue from participating patients. As of right now, beta sites have been identified, and beta projects are already underway.

"Genomics and biomarkers are key to unlocking further prognostic and predictive ability," Dr. Heng concluded.

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