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IL-2 for Kidney Cancer Offers Cure, but Needs to Be Given by Experts

Pam Harrison | May 12, 2014

Although high-dose interleukin-2 (HDIL-2) is currently not used often in the treatment of metastatic renal cell carcinoma (mRCC), the toxicity can be managed by expert centers, and it offers the only potentially curative treatment for patients with advanced disease.

A retrospective study of 88 patients from 1 such center, published online on April 21 in *Urology*, reports that 60% of patients were still alive at 2 years, and 4 patients (4.5%) had a complete response after treatment with only HDIL-2.

"I am one of the few people who stands up at kidney cancer meetings and waves the flag for IL-2," lead author Thomas Schwaab, MD, PhD, assistant professor of urology and immunology, Roswell Park Cancer Institute, Buffalo, New York, told *Medscape Medical News.*

"Current targeted treatments all treat kidney cancer well in that they prolong regression, but none of them have a truly curative aspect to them. Our clinical results continue to be impressive in this otherwise lethal disease," he said in an intereview.

The study followed a cohort of 88 patients with mRCC who received 1 cycle or more of HDIL-2 therapy. First author Michael Hanzly, DO, and colleagues from the Roswell Park Cancer Institute report that the median progression-free survival (PFS) was 8.6 months.

Overall survival (OS) for the cohort was prolonged to 35.5 months.

The median duration for patients who achieved stable disease on HDIL-2 treatment was 24.2 months.

Treatment was associated with important toxicities, but as the authors suggest, toxicities can be both anticipated and expertly managed in centers such as the Roswell Park Cancer Institute, which has experience treating patients with HDIL-2.

Requires "High Level of Experience"

Asked by *Medscape Medical News* to comment on the study, Nicholas Vogelzang, MD, Comprehensive Cancer Centers of Nevada, in Las Vegas, noted that he still recommends HDIL-2 to patients with excellent performance status and who are younger than 60 years.

Indeed, his colleague in Las Vegas, Wolf Samlowsi, MD, who is also affiliated with the Comprehensive Cancer Centers of Nevada, is in the process of treating one of his own patients with HDIL-2 therapy now.

"We both agree that IL-2 still has a role [in mRCC] and that it does offer a curative potential, [although] in fewer than 10% of patients treated," he said.

Nevertheless, HDIL-2 therapy requires "a high level of experience, inpatient close monitoring by skilled nurses, and a physician willing to take on the heavy burden imposed by an around-the- clock risk of toxicity," Dr. Vogelzang added.

"This is why less than a thousand patients per year in the US receive the drug," he said.

Renal Cell Carcinoma

In their article, the researchers note that a total of 906 patients with renal cell carcinoma (RCC) were treated at the Roswell Park Cancer Institute between 2004 and 2011.

Out of 167 patients with mRCC, 91 were treated with HDIL-2 monotherapy, and 88 patients were evaluable for subsequent analysis.

"Pretreatment glomerular filtration rate ranged from 41 to 88 mL/min," the authors note.

Almost 15% of patients had impaired renal function prior to initiation of HDIL-2 therapy, they add. Impaired renal function was defined as a serum creatinine level >1.5 mg/dL.

Recombinant IL-2 was given intravenously at a dose of 600,000 IU/kg during a 15-minute bolus every 8 hours for a maximum of 14 doses.

Each treatment cycle consisted of a total of 2 courses of HDIL-2, given on days 1 to 5 and again on days 15 to 19.

Cycles were separated by 6 to 8 weeks, and subsequent cycles were given only in those patients who had an objective response to treatment or whose disease had stabilized following HDIL-2 administration.

All patients received levofloxacin 250 mg each day, given prophylactically along with standard supportive medications, including antipyretics, antiemetics, antihistamines, and antidiarrheals.

Patients who developed hypotension on HDIL-2 therapy were treated with intravenous boluses of saline or albumin.

"Analysis of patients with pre-HDIL-2 renal impairment showed that 92.3% of these patients received > 1 treatment cycle, whereas only 50.6% of patients with adequate initial renal function received 2-3 cycles," as the authors note.

Patients with renal impairment prior to initiation of treatment had a comparable median OS at a median of 36 months compared with 27.2 months for those with adequate initial renal function.

Four patients, or 4.5% of the group overall, achieved a complete response (CR); 10 patients, or 11.4%, achieved a partial response (PR), and disease stabilized in 28 patients, or 31.8% of the group overall.

Additional Therapies

The investigators point out that 18 patients received HDIL-2 as the only treatment for their mRCC.

Another 7 patients received different treatment modalities prior to receiving treatment with HDIL-2, and 43 patients received additional treatment after being treated with HDIL-2. Sunitinib (*Sutent*, C. P. Pharmaceuticals International CV) was used in 63% of patients who received additional treatment after receiving HDIL-2 therapy.

"Of these different groups, those who received HDIL-2 followed by additional targeted therapy showed the best PFS and OS," investigators report.

In contrast, those who received treatment before HDIL-2 had a poorer prognosis. The mean number of treatment courses in this patient group was 2.

Table. Treatment Response by Additional Therapies

	Additional Treatment Prior to HDIL-2 Initiation	**Additional Treatment After HDIL-2 Initiation**
Progression-free survival	4.8 months	13.2 months
Overall survival	5 months	40 months

Median PFS and OS in the HDIL-2 alone group were 8.4 and 29.5 months, respectively; at 2 years, some 57% of this subgroup was still alive.

The 4 patients who achieved a complete response (4.5%) had received HDIL-2 therapy alone.

"If you've ever seen a patient with metastatic kidney cancer with a complete response, you become a firm believer," Dr. Schwaab commented.

Toxicity of HDIL-2

As Dr. Schwaab noted, HDIL-2 therapy does have a "distinct" side effect profile.

For example, more than two thirds of the cohort developed hypotension. Liver enzyme elevations were observed in more than 42% of patients, and fever and chills occurred in one third or more of HDIL-2 recipients.

Serum troponin-I levels were also elevated in about one fifth of the group, and more than 12% experienced diarrhea.

Overall, almost 64% of adverse events (AEs) reported were grade 3 toxicities, and 8% were grade 4.

"One of the toxicities of HDIL-2 is renal toxicity, and the textbook teaching is that if you have impaired kidney function, you are not going to be a candidate for HDIL-2," Dr. Schwaab said.

In their own experience, however, "we became more and more comfortable treating patients even with impaired renal function, to the point where if a patient had impaired renal function and was receiving HDIL-2, they were so well managed that they actually completed all their treatment cycles," he added.

When renal impairment did occur — as it did in 63% of the group overall — it was temporary, he added, and all patients returned to pretreatment baseline renal function levels following termination of IL-2 therapy.

"I think if you are being treated at an institution that's had a lot of experience with HDIL-2, the side effect profile can be really well managed, and we did not have any mortality in our patient population, and I think that reflects the fact that we know very well how to give IL-2," Dr. Schwaab said.

"So this data tells us that in our specialized setting, we can safely provide this treatment to more patients, even those with chronic renal insufficiency," he added.

The authors and Dr. Vogelzang have declared no relevant financial relationships.

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