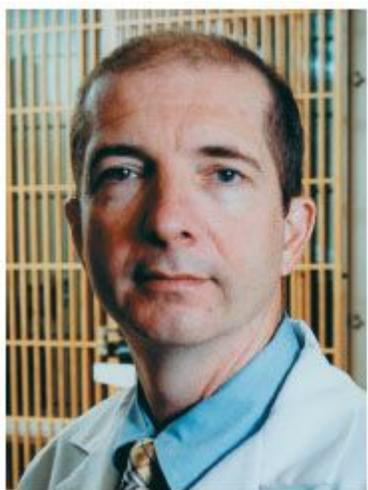


Avastin/sunitinib RCC trial closes after serious toxicities

Genitourinary Cancers, Renal Cell Carcinoma, Cancer Complications



“This is the way the process is supposed to work.”

— **DR. ROBERT MOTZER** the drug was terminated.

By Steven K. Wagner

The lead investigator in an evaluation of bevacizumab (Avastin) combined with sunitinib malate (Sutent) for renal cell carcinoma (RCC) said the project would be abandoned. FDA issued a product safety alert after Genentech, Avastin’s developer, reported serious complications in several patients enrolled in the phase I trial.

“In my opinion, this particular trial is not going to go anywhere in renal cell cancer,” said **Robert Motzer, MD**, of Memorial Sloan-Kettering Cancer Center.

In its July 14 alert, FDA declared, “Avastin is not approved for use in combination with sunitinib malate, and this combination is not recommended.” The alert was based on a July 11 letter from Genentech to cancer care specialists.

Dr. Motzer told ONI that he was surprised by the complications, which included microangiopathic hemolytic anemia (MAHA) with severe hypertension. Initially, tumor response was excellent, and the full dose was reached without dose-limiting toxicity, he said. But over time, poor tolerance became apparent. All patients who developed MAHA recovered when the drug was terminated.

Poor tolerability that did not involve MAHA led Genentech to close two phase II trials of Avastin/sunitinib in NSCLC and metastatic breast cancer. Genentech spokesperson **Kimberly Ocampo** said the negative results would not affect the overall Avastin development program.

Dr. Motzer noted that the cases of MAHA in his study were observed in patients who received the highest dose level of sunitinib malate. “One could potentially look at alternative dosing strategies with very low doses or intermittent doses in clinical trials,” he said.

The phase I dose-escalation study involved 25 patients in three cohorts. Five of 12 patients received the highest sunitinib dose, and two of those subjects had severe MAHA.

Dr. Motzer theorized that the drugs may have caused a reaction in the blood vessel lining or that the complications may be unique to RCC patients. The trial marked the first time he had seen MAHA in RCC patients, he said.

Dr. Motzer noted that, despite the disappointing outcome, “this is the way the process is supposed to work. If there is a signal like this, we need to act on it. That’s exactly what we did in a strong fashion.”

- See more at: <http://www.cancernetwork.com/articles/avastinsunitnib-rcc-trial-closes-after-serious-toxicities#sthash.jHLvsK0o.dpuf>