

IN EVERY ISSUE

# Kidney Cancer & Prostate Cancer

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## Third Targeted Drug Approved for Kidney Cancer

Torisel (temsirolimus) joined the ranks of Sutent (sunitinib) and Nexavar (sorafenib) on May 30 as the latest approved targeted agent to treat advanced stages of renal cell carcinoma, or RCC, the most common type of kidney cancer. Of the more than 50,000 RCC cases each year, about 40,000 are diagnosed in advanced stages.

The Food and Drug Administration based its decision primarily on a phase III study comparing three arms: Torisel alone, interferon alone, and a combination of Torisel and interferon in patients with metastatic RCC. Interferon is considered the standard therapy for metastatic RCC, but experts say Sutent is now more commonly used in these patients.

Patients who received Torisel alone had a median overall survival of 10.9 months compared with 7.3 months in the interferon arm, a significant increase of nearly 50 percent. Researchers noted the combination was not as effective as Torisel alone—median overall survival in the combination arm was only 8.4 months—possibly the result of treatment delays caused by interferon’s side effects. A significant improvement in time to progression was seen with Torisel alone (5.5 months) compared with interferon alone (3.1 months). Side effects in the Torisel-only arm were less severe and included rash and anemia.

Unlike Sutent and Nexavar, which target the vascular endothelial growth factor (secreted by tumor cells to signal blood vessel growth to the tumor), Torisel inhibits another key protein involved in tumor survival and growth called mammalian target of rapamycin, better known as mTOR. Torisel—the first drug to show an increase in survival for metastatic RCC—is also being studied in mantle cell lymphoma, breast cancer, and ovarian cancer. For more on Torisel, go to [www.wyeth.com](http://www.wyeth.com)

## Approval Decision Alters Fate of Immunotherapy Agent

Immunotherapy uses the body's immune system to identify cancer cells and destroy them, and in early May, one such treatment received an unwelcome verdict from the Food and Drug Administration.

Provenge® (sipuleucel-T) for hormone-refractory prostate cancer was reviewed before the independent Cellular, Tissue and Gene Therapies Advisory Committee for the Center for Biologics Evaluation and Research in March. Advisory committees recommend to the FDA if a drug should be approved, but the FDA does not necessarily act in agreement, as demonstrated with Provenge's case. Although the majority of advisory committee members voted in favor of Provenge's approval (13 to 4), the FDA said in May that current data do not confirm effectiveness and asked Dendreon Corporation, maker of Provenge, for more data, which will likely come from the IMPACT trial, either with positive interim data in 2008 or with its completion in 2010.

Provenge stood to be the first vaccine approved to treat cancer. It's specifically designed to treat advanced prostate cancer that is no longer responsive to hormone therapies. Of the more than 200,000 prostate cancer diagnoses this year, hormone-refractory prostate cancer patients make up about 45,000 to 55,000 cases.

Critics of the vaccine say current studies have not provided substantial evidence that Provenge prolongs survival, and although a phase III study suggests patients receiving the vaccine survived four months longer, overall survival was not specifically studied in that trial—it was only observed after the interim data were analyzed. What was being studied in that trial, time to progression, did not statistically differ between the control and Provenge groups. A smaller study of similar design evaluated by the FDA did not show a difference in time to progression or overall survival. Side effects were limited to temporary flu-like symptoms. For more on Provenge, go to [www.dendreon.com](http://www.dendreon.com)

### First Agent Approved to Prevent Clots in Cancer Patients

Fragmin (dalteparin) became the first drug to prevent recurrent blood clots in cancer patients when it was granted expanded approval for the indication in May. Although an uncommon side effect—about 1 to 2 percent of all cancer patients (14,000 to 28,000) develop blood clots—cancer patients are seven times more likely to develop a blood clot than someone without cancer.

Blood clots, including deep vein thrombosis, or DVT (blood clots formed in the legs or pelvic region), and pulmonary embolism (blood clots formed in the lungs), develop because cancer cells or treatments, including chemotherapy and surgery, can increase blood-clotting proteins and platelets, weaken vessel walls, or produce fewer proteins called anticoagulants that thin the blood. Surgery may also immobilize patients, predisposing them to blood clots. Fragmin inhibits thrombin, a blood-clotting protein, to prevent development of a new clot or the swell of an already existing one.

The approval was based on data from a study published in 2003 comparing patients receiving Fragmin injection once a day for six months with those receiving the agent for five to seven days followed by warfarin (also known as

Coumadin), an oral anticoagulant, for six months. Patients receiving only Fragmin experienced about 50 percent fewer blood clots than patients receiving warfarin (8 percent compared with 16 percent).

Side effects of Fragmin, which was originally approved in 1994 to prevent DVT in patients undergoing hip replacement or abdominal surgery, include risk of bleeding and bruising. For more on Fragmin, go to [www.fragmin.com](http://www.fragmin.com)

### Vectibix Trial Comes to a Halt

Amgen's phase III study of a triple combination of Vectibix (panitumumab), Avastin (bevacizumab), and chemotherapy as first-line treatment in metastatic colorectal cancer has been stopped. Preliminary data from the PACCE (Panitumumab Advanced Colorectal Cancer Evaluation) trial showed the control arm receiving only Avastin and chemotherapy had better progression-free and overall survival rates than the Vectibix arm. The trial's primary goal was to increase progression-free survival, but also improve overall survival, response rate, and safety. Interim results also showed an increased risk of severe side effects, such as diarrhea, dehydration, and infection, in the Vectibix arm. Patients receiving Vectibix in the trial were offered the option of continuing in the other arm of the study while investigators further review the data.

Vectibix, approved in September 2006 for second-line treatment of metastatic colorectal cancer, is the first fully human monoclonal antibody approved to inhibit the epidermal growth factor receptor. Researchers estimate up to 77 percent of colorectal cancers overexpress EGFR. Researchers hope results from an early-phase lung cancer trial with Vectibix and the investigational drug motesanib diphosphate (formerly AMG 706) will help explain why the PACCE trial failed. Motesanib diphosphate, a drug similar to Avastin that targets the vascular endothelial growth factor receptor, is being combined with Vectibix and standard chemotherapy in a regimen much like that of the PACCE trial, allowing scientists to better examine the combined effects of EGFR inhibitors, antiangiogenic therapy, and chemotherapy.

The results of the PACCE trial do not affect any other ongoing trials or its current approval. The drug is still being tested in phase III trials in combination with chemotherapy as first- or second-line treatment. Side effects commonly seen with Vectibix include rash, diarrhea, and fatigue. For more on Vectibix, go to [www.vectibix.com](http://www.vectibix.com).