New data on sunitinib clarifies dosing schedule
ORLANDO, FL—Data presented at the 2011 ASCO GU Cancer Symposium from the phase 2 Renal EFFEC T trial adds to the established clinical experience and supports the dosing profile of sunitinib (Sutent®). The safety profile observed in patients treated with a regimen of 37.5 mg continuous daily dosing compared with the approved treatment cycle of 50 mg daily, given on a 4 weeks on, 2 weeks off treatment schedule, were similar. Efficacy endpoints, such as overall response rate and overall survival (OS) showed similar results between the 2 doses, while a trend toward inferior time to disease progression was noted with the continuous dosing regimen. In addition, data from a retrospective, exploratory analysis of 5 sunitinib clinical trials in advanced renal cell carcinoma (RCC) suggest that development of treatment-induced hand-foot syndrome (HFS) may serve as a predictive biomarker of efficacy. According to findings from this analysis, patients with advanced RCC who developed sunitinib-associated HFS had a significantly better clinical outcome than those who did not develop HFS, with respect to all efficacy endpoints analyzed, including progression-free survival (PFS) and OS. Overall, patients who did not develop HFS still had substantial benefit from sunitinib, although the presence of HFS identified a subset of patients who had better efficacy on treatment. While additional prospective studies are needed to validate these findings, these data contribute to a growing body of knowledge regarding the adverse effect profile for Sutent and potential correlations with efficacy.

Marketing rights for new adjuvant agent granted to Prometheus Laboratories
MUNICH—WILEX AG has announced the granting of US commercialization rights for RENCA REX® (girentuximab) to Prometheus Laboratories Inc, San Diego. Prometheus is an established specialty pharmaceutical and diagnostics company with a proven track record in gastroenterology and oncology. Prometheus will co-fund a portion of the ongoing development of RENCAREX, which is a phase 3 product candidate for adjuvant use in non-metastatic clear cell renal cell cancer. The deal includes the potential development in further indications. Prometheus markets Proleukin®, an oncology product indicated for metastatic renal cell carcinoma and metastatic melanoma, in the United States. If RENCAREX receives FDA approval, Prometheus would be able to offer a treatment for both adjuvant and metastatic kidney cancer.

Renal cancer drug temsirolimus shows promise against mesothelioma
DENVER, CO—Temsirolimus may increase the effectiveness of chemotherapy for mesothelioma, according to a study published in the May issue of the Journal of Thoracic Oncology. Temsirolimus, a kinase inhibitor, blocks the action of mammalian target of rapamycin (mTOR), a protein that regulates cell growth, which can slow tumor growth. It is used to treat advanced renal cell carcinoma. But researchers in Austria have found that temsirolimus may also slow the growth of malignant pleural mesothelioma cells. Mesothelioma, a cancer that is usually caused by exposure to asbestos and may not appear until 30 to 50 years after exposure, frequently resists chemotherapy and radiation treatment.

The researchers found that temsirolimus strongly blocked mTOR-mediated signals and had a cytostatic, or growth-stopping, effect on all mesothelioma cells. However, mesothelioma cells that were resistant to cisplatin, a widely used chemotherapy drug, showed hypersensitivity against temsirolimus. This suggests that mTOR inhibitors such as temsirolimus might provide a promising treatment strategy either in combination with chemotherapy or as second-line treatment after chemotherapy failure.

Kidney cancer on the rise: improved detection, obesity epidemic may play role
ORLANDO, FL—The number of people with kidney cancer in the United States has risen steadily since 1975 and, since 1991, the greatest increase has been among younger people. From 1975 to 1990, the number of new cases increased on average by 3.6% annually, says study leader Kenneth G. Nepple, MD, a fellow in urologic oncology at Washington University in St. Louis. From 1991 to 2006, cases rose on average by 2.9% per year. Nepple told WebMD that cases increased in all age groups from 1975 to 2006. But the proportion of patients diagnosed when they were younger than age 65 increased from 45.9% in 1991 to 55.3% in 2006, according to information presented at the 2011 GU Cancers Symposium. Some of the rise comes from increased detection on CT scans, says Christopher G. Wood, MD, Professor of Urology at the University of Texas M.D. Anderson Cancer Center in Houston. The researchers used data from the National Cancer Institute’s Surveillance, Epidemiology, and End Results cancer registry database to look at renal cancer trends from 1975 to 2006. The database covers about one-fourth of the US population.

Hepatitis C tied to higher kidney cancer risk
DETROIT—New research suggests that the hepatitis C virus is linked to a much higher risk of developing kidney cancer. A study of more than 67,000 patients enrolled in the Henry Ford Health System from 1997 through 2008 found that 0.6% of patients with hepatitis C developed kidney cancer, double the rate of other patients, and the increased risk (continued on page 41)
remained after researchers adjusted for factors such as age, sex, and race.

“These results add to growing literature that shows that the hepatitis C virus causes disease that extends beyond the liver,” said lead author Stuart C. Gordon, MD, Director of Hepatology at Henry Ford Hospital. Gordon said it is too early to determine whether more kidney cancer screening of people with hepatitis C is needed. “However, a heightened awareness of an increased kidney cancer risk should dictate more careful follow-up of incidental renal [kidney] defects when detected on imaging procedures in patients with chronic hepatitis C,” Dr Gordon stated. The study appeared in the journal Cancer Epidemiology, Biomarkers & Prevention.

Newly discovered mutations may help drive common kidney cancer

HINXTON, UK—Researchers have discovered mutations in the gene PBRM1 in more than one-third of clear cell renal cell carcinomas (ccRCC), the most common kidney cancer. In a series of experiments led by Dr Ignacio Varela of the Wellcom e Trust Sanger Institute, an international team of researchers identified PBRM1 as a potential tumor suppressor gene and showed that the loss of the gene’s function may contribute to kidney cells developing the properties of cancer cells, such as uncontrolled cell growth. The findings appeared online in Nature.

The scientists first sequenced portions of the genome known to produce proteins (the exome) in 7 ccRCC tumor samples and normal tissue from the same patients. They identified 156 mutations in the 7 samples, but only mutations in the PBRM1 gene were found in more than 1 sample. They next sequenced the PBRM1 gene in an additional 257 RCC samples (including 36 non-ccRCC cases) and found mutations in 88 samples (all ccRCC), a frequency that the authors described as “remarkable.” The researchers also found PBRM1 gene mutations in breast, lung, kidney, gallbladder, and pancreatic cancer cell lines. Analysis of genetic data from a mouse model of pancreatic cancer indicate that inactivation of the PBRM1 gene may help drive pancreatic tumor development in this model.

Using small interfering RNAs to block PBRM1 gene activity in ccRCC cells, the researchers were able to increase cell proliferation cell-colony formation (the ability to grow and divide without physical support), and cell movement. Similar to that required for metastasis, PBRM1 codes for a protein that is involved in chromatin remodeling, a process that allows transcription factors to gain access to DNA that is otherwise tightly packaged with proteins. According to the researchers, analysis of the cell-signaling pathways regulated by PBRM1 suggests that, “PBRM1 activity regulates pathways associated with chromosomal instability and cellular proliferation.” They also noted that several other genes that have been implicated in ccRCC are involved in chromatin remodeling. “This is very promising, very exciting work,” commented Marston Linehan, MD, Chief of the Urologic Oncology Branch in NCI’s Center for Cancer Research. Dr Linehan was part of the scientific team that identified the tumor suppressor gene VHL, which is the only other gene known to play a role in a large number of ccRCC cases. He concluded that “This finding leads us potentially into a whole new direction in thinking about the basic aspects of kidney cancer and potential approaches to therapy. It’s possible that mutations in PBRM1 are a critical part of clear-cell kidney cancer and that you need both VHL and PBRM1 to be altered to develop a clear-cell kidney cancer.” KCJ