ALEXANDRIA, Va. – Studies released today in advance of the 2014 Genitourinary Cancers Symposium reveal survival outcomes in multiple GU cancers and provide insights on the early termination of cancer clinical trials. This year marks the 10th anniversary of the Symposium, which will be held January 30 – February 1 at the San Francisco Marriott Marquis.

Four key studies were presented in today’s presscast:

- **Enzalutamide Improves Survival in Men with Metastatic Castration-Resistant Prostate Cancer**: Presented in full for the first time, results from the phase III PREVAIL study show that enzalutamide increases survival by 29 percent in men with metastatic castration-resistant prostate cancer and slows or stops cancer growth in 59 percent of patients, delaying the need for chemotherapy by 17 months.

- **Long-Term Data Confirms Radiotherapy Plus Anti-Androgen Therapy Substantially Improves 10- and 15-Year Prostate Cancer Survival Rates**: An updated analysis of clinical trial data from the Scandinavian Prostate Cancer Group’s Study VII shows that the combination of radiotherapy and oral anti-androgen therapy more than halves the 10- and 15- year cancer-specific mortality rate for men with locally advanced prostate cancer.

- **Common Drug Improves Survival in Hypertensive Patients with Metastatic Renal Cell Carcinoma**: A retrospective study shows that angiotensin system inhibitors (ASIs), medications commonly used for hypertension, improve survival by nine months for patients with metastatic renal cell carcinoma who also have high blood pressure.

- **Early Termination Not Unique to Genitourinary Cancer Clinical Trials - Approximately One in Five Adult Cancer Clinical Trials Fails to Complete**: Analysis of data from Clinicaltrials.gov shows that the early termination of clinical trials is not unique to genitourinary trials. Approximately one in five cancer clinical trials fails to complete, most commonly due to poor accrual.
"The studies highlighted today present clinicians with a number of thought-provoking and potentially practice-changing implications," said Charles J. Ryan, MD, moderator of today’s presscast, “Many of which can be integrated into our daily clinical practice and future research efforts.”

Genitourinary cancers include those of the prostate, kidney, bladder, and testis, as well as less common cancers such as those of the penis, ureters, and other urinary organs. In 2014, more than 385,000 people in the United States are expected to be diagnosed with genitourinary cancers, with an estimated 60,500 deaths. The most common genitourinary cancer is prostate cancer, which according to estimates, will be diagnosed in 233,000 men in the United States in 2014 and claim more than 29,400 lives.[i]

The 2014 Genitourinary Cancers Symposium is co-sponsored by the American Society of Clinical Oncology (ASCO), the American Society for Radiation Oncology (ASTRO) and the Society of Urologic Oncology (SUO).

Enzalutamide Improves Survival in Men with Metastatic Castration-Resistant Prostate Cancer

(Summary contains updated data not included in the abstract)

Results from the phase III PREVAIL study show that the androgen-receptor blocker enzalutamide increases survival by 29 percent in men with metastatic castration-resistant prostate cancer (mCRPC) and delays progression of the disease by 81 percent. While preliminary results from this study were released in October 2013 after the Independent Data Monitoring Committee recommended that the study be stopped early, the data were presented in full for the first time at the GU Cancers Symposium.

“Enzalutamide is likely to become an important new treatment option that has a significant impact on the progression of prostate cancer,” said lead author Tomasz Beer, MD, FACP, professor of medicine and deputy director of the Knight Cancer Institute at Oregon Health and Science University. “If approved for this indication, it will become an important standard option for use before chemotherapy in patients with asymptomatic or minimally symptomatic advanced prostate cancer.”

In this double-blind, placebo-controlled phase III study, 1,717 men with mCRPC who had not previously received chemotherapy were randomized to receive enzalutamide or a placebo plus standard hormone therapy. The participants had previously received treatment for the primary tumor, such as surgery or radiation therapy, as well as hormone therapy with an LHRH agonist or a first-generation anti-androgen. The two primary endpoints are overall survival and radiographic progression-free survival. Radiographic progression free survival uses regular bone and CT scans to monitor for cancer growth.

The results showed that enzalutamide slowed or stopped cancer growth in 59 percent of patients (20 percent complete responses and 39 percent partial responses), compared with five percent of patients in the placebo arm. In addition, enzalutamide significantly delayed the need for chemotherapy. On average, patients receiving enzalutamide needed chemotherapy 17 months later than those in the placebo arm. Based on this positive interim data, the Independent Data Monitoring Committee recommended that patients on the trial receiving the placebo be offered enzalutamide.

Enzalutamide is a second generation androgen-receptor blocker, which offers more potent activity than the first generation of these agents – bicalutamide, flutamide, and nilutamide. The most
common side effects included fatigue, constipation, and back and joint pain, in addition to side effects associated with hormone therapy, such as weight gain and hot flashes. Overall, enzalutamide was well tolerated – the same percentage (six percent) of patients taking enzalutamide and the placebo left the study due to side effects.

**Long-Term Data Confirms Radiotherapy Plus Anti-Androgen Therapy Substantially Improves 10- and 15-Year Prostate Cancer Survival Rates**

An updated analysis of clinical trial data from the Scandinavian Prostate Cancer Group’s Study VII showed that adding radiotherapy to oral anti-androgen therapy, a type of hormone therapy, more than halved the 10- and 15-year prostate cancer-specific mortality rates for men with locally advanced prostate cancer, compared to anti-androgen therapy alone.

“When this study started in 1996, the standard treatment was hormone therapy alone, but this trial continues to show that adding radiotherapy substantially boosts long-term survival,” said lead author Sophie Dorothea Fosså, MD, a professor in the department of oncology at Oslo University Hospital in Norway. “This combination more than doubles the 10-year survival rate and confirms that this approach should be a standard option for men with this type of prostate cancer who are expected to live at least another 10 years.”

After almost eight years of observation, results published in 2009 showed a 12 percent reduction in prostate cancer-specific mortality in patients with locally-advanced prostate cancer who initially received one injection of testosterone-removing hormone treatment that lasts for three months followed by two months of radiotherapy and continuous pill-based hormone therapy, compared with those who received hormone therapy alone.

Locally-advanced prostate cancer is defined as cancer that has grown through the prostate capsule that covers most of the organ. When this study began, this type of prostate cancer was considered inoperable, and surgery is still not often used because it may be difficult to remove all of the cancer. Radiotherapy can be directed at tissue beyond the prostate and is able to kill cancer cells outside the capsule.

In this updated analysis, after 11 years of observation, researchers reviewed mortality data from Norwegian and Swedish death registries. Among the 439 men receiving hormone therapy alone, 118 died of prostate cancer, compared with 45 out of 436 men receiving the combination treatment. For the men receiving hormone therapy alone, the 10- and 15-year prostate cancer-specific mortality rates were 18.9 percent and 30.7 percent, respectively. For those receiving the combination, these rates were 8.3 percent and 12.4 percent.

Both hormone therapy and radiotherapy cause side effects, such as impaired sexual function and minor bowel problems. Dr. Fosså added that it is important to assess each patient’s acceptance of the side effects and priorities when discussing treatment options so patients are comfortable with their expected post-treatment quality of life.

**Common Drug Improves Survival in Hypertensive Patients with Metastatic Renal Cell Carcinoma**

According to a retrospective study, the use of angiotensin system inhibitors (ASIs), such as lisinopril, captopril, and losartan, improved the survival of patients with metastatic renal cell carcinoma (RCC) by nine months, compared with patients who were not receiving these types of agents. Survival was even higher in patients receiving ASIs along with treatment targeting the VEGF pathway. Hypertension is a common condition in the United States, and this is the largest analysis to date evaluating the role of ASIs on outcomes in patients with cancer.

“Though larger prospective studies are needed, based on the results of this study, an ASI should be considered for patients with metastatic renal cell carcinoma who need an antihypertensive and do not have any contraindications that preclude their use, especially in patients receiving VEGF targeted treatments,” said lead author Rana McKay, MD, a clinical oncology fellow at Dana Farber Cancer Institute in Boston, Mass. “However, it is too early to determine if ASIs should be used for
patients with metastatic renal cell carcinoma who do not also have hypertension or another medical condition to warrant ASI treatment.”

Researchers reviewed information from a clinical trials database of 4,736 patients with metastatic renal cell carcinoma treated on phase II and III clinical trials sponsored by Pfizer, Inc. ASI users were defined as patients taking an ASI when they started treatment or within the first 30 days of treatment. The cancer treatments reflected the current treatments being used and researched for RCC and varied to include VEGF targeted agents (such as sunitinib, sorafenib, axitinib, bevacizumab), mTOR-targeted agents (temsirolimus), and interferon.

The overall survival for patients receiving ASIs was 27 months, compared with 17 months for non-ASI users. In addition, the cancer was more likely to shrink in patients taking ASIs. Researchers also analyzed data from patients taking any type of antihypertensive (2,000 patients) and found that the overall survival for patients using ASIs was 27 months compared to 18 months for those on other types of anti-hypertensive agents. When evaluating patients based on therapy type, the benefit of ASIs was most significant in patients treated with VEGF-targeted therapy when compared with mTOR-targeted therapy or interferon.

Angiotensin system inhibitors fall into two classes - angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs). An ACE inhibitor lowers blood pressure by reducing the production of angiotensin II, which increases blood pressure, whereas ARBs block the effect of angiotensin II at the receptor. Increasingly, research has indicated that the peptide hormone angiotensin II is involved in certain steps in the process of carcinogenesis, including angiogenesis. Overall, ASIs are commonly used medications in the United States. They are generally well-tolerated; however, side effects include fatigue, low blood pressure, dizziness, increased potassium levels, cough, and angioedema (an allergic reaction).

**Early Termination Not Unique to Genitourinary Cancer Clinical Trials - Approximately One in Five Adult Cancer Clinical Trials Fails to Complete**

An analysis of 7,776 adult cancer clinical trials registered on Clinicaltrials.gov showed that approximately 20 percent of trials failed to complete (for reasons unrelated to the efficacy or side effects of the intervention). In 2010, a report from the Institute of Medicine entitled “A National Clinical Trials System for the 21st Century” called attention to this potential problem, indicating that about 40 percent of the clinical trials initiated by the NCI Cooperative Groups are never finished. However, NCI cooperative trials account for a small proportion of all cancer clinical trials and the scope of this problem within the larger clinical trials enterprise had not previously been comprehensively examined, providing the rationale for the current analysis.

“When we consider what prevents the translation of clinical trials to new standard treatments for our patients, we generally think of two things – an experimental intervention doesn’t work and/or the side effects are too severe,” said senior author Matthew Galsky, MD, associate professor of medicine at the Icahn School of Medicine at Mount Sinai and the director of the Genitourinary Medical Oncology Program at the Tisch Cancer Institute. “However, our findings reveal a third major barrier to progress in cancer care – that a large proportion of initiated clinical trials are not completed at all, failing to contribute to our understanding of how best to care for patients.”

In this study researchers analyzed data from Clinicaltrials.gov for all phase II and III adult cancer clinical that were registered between 2005 and 2011. They identified 7,776 trials. Those that were designated as “stopped early” in the registry were classified as failing to complete. Using statistical methods to account for the different time frames during which trials were initiated and closed, they determined that approximately 20 percent failed to complete.

Overall, poor accrual was the most common cause of trials failing to complete, accounting for almost 40 percent of these trials. The researchers initially became interested in studying this topic after noting that a series of clinical trials in bladder cancer failed to complete, leading to a poor level of evidence to guide treatment decisions in this disease. However, in the current study, they found that genitourinary cancer trials, including bladder cancer trials, were no more likely to fail to complete than trials in other cancer types. Researchers found that trials conducted at a single
location, trials with industry sponsors, and trials with study locations only inside the United States were more likely to fail to complete.

According to Dr. Galsky, “clinical trials that fail to complete waste financial resources and human capital. The results of this study further highlight the wide-ranging impact of poor accrual to cancer clinical trials in the United States.” As a clinical trialist himself, he notes that this is not an indictment of any other single stakeholder in the system but hopes that these findings will facilitate broader conversations regarding the need for new approaches to how trials are conducted and improve communication and collaboration among stakeholders to increase the efficiency of the system.

About ASCO:

Founded in 1964, the American Society of Clinical Oncology (ASCO) is the world’s leading professional organization representing physicians who care for people with cancer. With more than 35,000 members, ASCO is committed to improving cancer care through scientific meetings, educational programs and peer-reviewed journals. ASCO is supported by its affiliate organization, the Conquer Cancer Foundation, which funds groundbreaking research and programs that make a tangible difference in the lives of people with cancer. For ASCO information and resources, visit asco.org. Patient-oriented cancer information is available at Cancer.Net.