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THE
# CLINICAL CANCER LETTER

*Cancer research news for clinicians*

*Kidney Cancer*

## GSK's Pazopanib Benefits Similar to Sunitinib; Sponsor Points to More Favorable Safety Profile

In an international, phase III, head-to-head trial, pazopanib and sunitinib had similar benefits in progression-free survival, but safety profiles and several quality of life measures favored pazopanib in patients with advanced renal cell cancer, pazopanib sponsor GlaxoSmithKline said.

The median time before the cancer progressed was comparable: 8.4 months for pazopanib (Votrient) and 9.5 months for sunitinib (Sutent). Median overall survival was also similar: 28.4 months for patients taking pazopanib and 29.3 months for sunitinib.

(Continued to page 2)

*Prostate Cancer*

## Radium 223 Dichloride Reduces Death Risk By 30 Percent in Castration-Resistant Disease

In the phase III ALSYMPCA trial of patients with castration-resistant prostate cancer and symptomatic bone metastases with no known visceral metastatic disease, radium 223 dichloride reduced the risk of death by 30.5 percent compared to placebo.

This overall survival benefit (HR=0.695) was observed in patients who were treated with the chemotherapy docetaxel prior to study enrollment and in those who were not. All patients in the study were treated with best standard of care in addition to radium 223 (Xofigo) or placebo.

(Continued to page 3)

*Ovarian Cancer*

## Survey Finds 70 Percent of Oncologists Prescribe Avastin Off-Label For Ovarian Cancer

A healthcare research and advisory firm found that Avastin is being prescribed off-label by about 70 percent of surveyed oncologists in first-line treatment of ovarian cancer.

Avastin (bevacizumab) is not approved by FDA for the treatment of ovarian cancer—but is frequently prescribed as an add-on agent to doublet platinum-based chemotherapy followed by continued administration of Avastin as a maintenance monotherapy. Avastin is approved in the European Union as first-line treatment for advanced ovarian cancer, as well as in conbination with chemotherapy for recurrent, platinum-sensitive ovarian cancer.

The research firm, Decision Resources, surveyed 103 medical

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## Phase III Head-to-Head Trial Shows Similar Benefits Between Votrient and Sutent

(Continued from page 1)

Pazopanib patients had a higher rate of liver enzyme abnormalities, in some cases leading to discontinuation of the drug. However, pazopanib patients had lower rates of blood cell abnormalities, hand and foot soreness, mouth sores, low thyroid activity, nausea, and fatigue.

Pazopanib was rated superior to sunitinib on 11 or 14 measures of quality of life. In addition, pazopanib patients had fewer phone consultations with providers and visited emergency rooms less frequently.

The study's findings were published in the New England Journal of Medicine.

The trial was sponsored by GlaxoSmithKline Pharmaceuticals, which manufactures pazopanib. Sunitinib is sponsored by Pfizer Inc. Both treatments are oral tyrosine kinase inhibitors and target multiple cell-surface tyrosine kinase receptors, including receptors for vascular endothelial growth factor.

FDA approved sunitinib in 2006 and pazopanib in 2009 as first-line treatments for advanced kidney cancer. The drugs previously demonstrated improved progression-free survival compared to Interferon or placebo.

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*Transplantation*

## CMX001 Reduces Adenovirus Progression and Viremia

Top-line data from a phase II study of CMX001 as preemptive therapy for adenovirus infection showed a potential benefit in reducing both progression to AdV disease and all-cause mortality compared to placebo.

In this trial of allogeneic hematopoietic cell transplant recipients, the 100 mg dose given twice weekly demonstrated decreased levels of AdV viremia, and also showed a potential benefit in reducing progression compared to CMX001 given once weekly.

Planned intent-to-treat analyses as well as exploratory analyses in specific patient groups were consistent in trends favoring the CMX001 twice-weekly regimen over placebo, although statistical significance was not established in this study.

AdV, a double-stranded DNA virus, causes respiratory infections including the common cold in healthy individuals. However, in patients with a compromised immune system such as those who have recently undergone bone marrow or organ transplants, AdV infections have a high mortality rate.

Because no antiviral is approved for use in AdV infection and based on the potential for antiviral activity from in vitro data, CMX001 was made available through an open-label protocol for exploratory use in over 100 patients with life-threatening AdV infections.

Results were presented at the European Group for Blood and Marrow Transplantation Meeting.

The study assessed the use of CMX001 at an earlier stage of AdV infection, when patients had detectable viremia but before the appearance of symptoms of disease.

Pediatric and adult patients who had recently undergone HCT and were found to have viremia without symptoms of AdV disease were randomized to one of three dosing regimens: CMX001 twice weekly, CMX001 once weekly, or placebo.

The primary endpoint was a composite of progression to symptomatic AdV disease or an increase of at least 10-fold in the levels of AdV in the blood. The study randomized 48 adult and pediatric patients.

CMX001 is an oral nucleotide analog lipid-conjugate that has shown broad-spectrum antiviral activity against all five families of dsDNA viruses that effect humans, including herpesviruses such as CMV, adenoviruses, polyomaviruses such as BK virus, papillomaviruses, and orthopoxviruses.

Full results from the phase II study have been

accepted for an oral late-breaker presentation at the Interscience Conference on Antimicrobial Agents and Chemotherapy on September 10 in Denver, Colo. CMX001 is developed by Chimerix Inc.

## Biomarker Identified Predicting Graft-Versus-Host Disease Risk

Researchers identified and validated a biomarker accessible in blood tests that could be used to predict which stem cell transplant patients are at highest risk for graft-versus-host disease.

The researchers found that patients with a high level of protein ST2 were more than twice as likely to have graft-versus-host disease that resisted standard treatment with steroids; and nearly four times as likely to die within six months of the transplant.

The findings were published in the New England Journal of Medicine.

Patients with low ST2 levels were more likely to respond to treatment regardless of how serious their graft-versus-host disease was graded, while patients with high ST2 levels were less likely to respond to treatment, whether their disease was graded less serious or more serious.

In addition, while the disease most commonly appears about 30 days after the transplant, higher ST2 levels in blood samples taken as early as 14 days after transplant were associated with an increased risk of death from the toxicity of the transplant, according to researchers.

The study authors noted that early identification of patients who likely won't respond to standard treatments is important and would allow physicians to consider additional therapies and early intervention, while patients with low risk will not need to have additional medicine further suppressing their immune system. But, they cautioned, additional large prospective studies are needed to better define the levels of risk predicted by the ST2 marker.



*Prostate Cancer*

## Radium 223 Reduces Death Risk By 30 Percent in Phase III Trial

(Continued from page 1)

Researchers performed both a pre-planned interim analysis (n=809) and an updated analysis (n=921) in this study. The overall survival benefit was the same in both analyses. The study was published in the New England Journal of Medicine. These data supported the FDA's approval of the Xofigo injection in May 2013.

Patients were stratified based on whether or not they had received docetaxel prior to study enrollment. The study treatment consisted of best standard of care and up to six intravenous injections of radium 223 or placebo each separated by an interval of four weeks.

The primary endpoint of the study was overall survival. A key secondary endpoint was time to first symptomatic skeletal event. The events were defined as first use of external beam radiation therapy to relieve skeletal pain, new symptomatic pathologic bone fracture, occurrence of spinal cord compression or tumor-related orthopedic surgical intervention.

The overall survival impact of radium 223 was consistent in both patients who received prior treatment with docetaxel and in those who did not. In the interim analysis, radium 223 reduced the risk of death by 25 percent (HR=0.755) compared to placebo in patients who received prior docetaxel treatment and by 39 percent (HR=0.611) compared to placebo in those who did not.

In the updated analysis, radium 223 reduced the risk of death by 29 percent (HR=0.710) compared with placebo in those who received prior docetaxel and by 26 percent (HR=0.745) compared with placebo in those who did not.

Radium 223 significantly improved OS in the overall study population at the interim analysis (HR=0.695, p=0.00185); median OS was 14 months with radium 223 plus best standard of care compared to 11.2 months with placebo plus best standard of care. These findings were supported by the updated analysis in which radium 223 showed the same significant improvement in OS (HR=0.695; median OS was 14.9 vs. 11.3 months).

In the interim analysis, radium 223 significantly prolonged the time to the first symptomatic skeletal event compared with placebo: a median 15.6 months compared to 9.8 months, respectively (HR=0.658, p<0.001). In addition, radium 223 significantly delayed the time to alkaline phosphatase progression (HR=0.167,

p<0.00001) and time to prostate-specific antigen progression (HR=0.643, p<0.00001).

Radium 223 is an alpha particle-emitting radioactive therapeutic agent with an anti-tumor effect on bone metastases, and is sponsored by Bayer HealthCare.

## Follow-up Finds Finasteride Reduces Prostate Cancer Risk Without Affecting Lifespan

A long-term follow-up to the Prostate Cancer Prevention Trial found that finasteride reduced the risk of prostate tumors by about 30 percent, and low-grade tumors by 43 percent, while having no impact on lifespan.

The 18-year follow-up to the study examined survival in both study arms to see if there was an increased risk of death in men who took finasteride. The results show no impact on either overall survival or survival after prostate cancer diagnosis.

The Prostate Cancer Prevention Trial began in 1993 and was coordinated by SWOG. The men in the finasteride arm had a median age of 62 and took the drug for seven years.

The data was published in the New England Journal of Medicine.

Finasteride is a generic drug developed and currently used by physicians to treat enlarged prostate and male pattern baldness. While it significantly reduces the risk of prostate cancer, during the trial of 19,000 men a slightly higher percentage of those on finasteride developed high-grade cancer than those taking a placebo, although this difference shrank in the follow-up analysis.

### *Ovarian Cancer*

## 70% of Surveyed Oncologists Prescribe Avastin Off-Label

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oncologists and 30 pharmacy and medical directors. Approximately half of the surveyed oncologists who prescribe Avastin in first-line advanced ovarian cancer indicate that they encounter reimbursement barriers, such as prior authorization, when prescribing Avastin in this setting.

In a report published by the U.S. Physician and Payer Forum, analysts found that current treatment of ovarian and endometrial cancers relies heavily on generically available chemotherapies and that carboplatin/paclitaxel is very frequently prescribed in early-stage ovarian cancer, first-line advanced ovarian cancer and in early-stage and advanced endometrial cancer.

However, the use of Avastin for treatment of ovarian cancer in all disease settings is common amongst surveyed oncologists and more than 65 percent of surveyed oncologists think that treatment rates with Avastin will increase in the next five years—primarily because they believe Avastin will gain regulatory approval for ovarian cancer, according to the report.

Avastin is rarely used by surveyed oncologists for treatment of endometrial cancer; however, surveyed oncologists believe that angiogenesis inhibitors can play a role in its treatment with 70 percent of surveyed oncologists responding that targeting the vascular endothelial growth factor pathway will likely be a promising treatment approach in this disease.

Avastin is sponsored by Roche and Genentech, and is approved by FDA for the treatment of metastatic colorectal cancer, metastatic renal cell carcinoma, glioblastoma, and non-small cell lung cancer.

### *Myeloma*

## Study Shows Early Treatment Of Asymptomatic Myeloma Can Improve Survival

A study conducted by the Spanish Myeloma Group showed that early treatment of asymptomatic myeloma can significantly improve the course of the disease, delay progression and increase patient survival.

The results show the need to identify patients with asymptomatic myeloma at high risk of developing the active form, and the advantages of considering this as an early symptomatic myeloma. Moreover, the possibility that early treatment in this phase can improve the subsequent course of multiple myeloma constitutes a change in paradigm in the routine clinical management of patients with this type of asymptomatic cancer, who until now did not receive any treatment if they did not present symptoms.

A total of 21 Spanish hospitals belonging to the Spanish Myeloma Group (GEM-PETHEMA) and three Portuguese centers have participated. The study was published in The New England Journal of Medicine.

A total of 120 individuals participated in the randomized trial and were divided into two groups: half of them did not receive any therapy until the appearance of myeloma symptomatology, the standard treatment

approach to date. The other 60, the experimental group, were given anti-myeloma treatment with lenalidomide in combination with dexamethasone.

In the experimental group, over 80 percent showed a response to the treatment. The risk of disease progression to symptomatic myeloma was 5.59 times lower in patients treated early compared to non-treated patients.

Around 74 percent of non-treated patients progressed to active myeloma while only 22 percent of patients treated early with lenalidomide and dexamethasone developed the active disease, according to researchers.

In the experimental group, 94 percent of patients receiving treatment were still alive at five years compared to 78 percent in the non-treated group, said researchers.

*Lymphoma*

## Pretreatment with Azacitidine Achieves 28-Month Remission

Patients with diffuse large B-cell lymphoma who took azacitidine with chemotherapy experienced a remission of their cancer and remained disease-free for as long as 28 months, according to a study.

Researchers found that pretreatment of aggressive lymphoma with azacitidine reawakens molecular cell death mechanisms that are shut off as the cancer progresses.

In a proof-of-concept, phase I study of 12 high-risk DLBCL patients, 11 achieved a complete remission of their cancer, and 10 remained cancer-free for up to 28 months. The patients were given low doses of azacitidine for five days before standard chemotherapy was used.

Azacitidine is a targeted drug approved for use in myelodysplastic syndrome. The study was published in Cancer Discovery and was led by researchers at Weill Cornell Medical College and NewYork-Presbyterian Hospital.

The researchers are expanding the study to additional DLBCL patients in a multi-center clinical trial that will soon enroll patients, and they also plan to study their pretreatment strategy in other tumor types, including additional lymphomas.

Azacitidine was chosen because of growing evidence that most cancers resist the killing powers of chemotherapy because of an inability to turn on cell death mechanisms. A major cause of this genetic resistance is the addition of silencing chemicals, called methyl groups, to death-inducing genes. These silencing chemicals prevent chemotherapy from activating the genes, making the treatment less effective. Azacitidine removes the methyl groups, allowing the chemotherapy drugs to activate these genes again and cause tumor cells to die.

*Non-Small Cell Lung Cancer*

## Specific Pathology Pattern Can Predict Recurrence

A study showed that a specific pattern found in the tumor pathology of some lung cancer patients is a strong predictor of recurrence.

According to the study's authors, the findings offer the first scientific evidence that may not only help surgeons identify which patients are more likely to benefit from less radical lung-sparing surgery, but which patients will benefit from more extensive surgery, potentially reducing the risk of lung cancer recurrence by 75 percent. The study was published in JNCI and led by researchers at Memorial Sloan-Kettering Cancer Center.

Researchers retrospectively evaluated the clinical characteristics and pathology information of 734 patients who had surgery for early-stage adenocarcinoma and found that tumors in 40 percent of those patients exhibited an abnormal cell pattern strongly associated with cancer recurrence after surgery.

No study to date has investigated the prognostic utility of this classification, called micropapillary morphology, for patients with small, early-stage lung adenocarcinomas. Currently there are no evidence-based criteria for choosing the most effective surgical approach for this group.

The findings suggest that limited resection may not be appropriate for patients with the pattern, as they were found to have a 34 percent risk of the cancer returning within five years after lung-sparing surgery, or limited resection, in which the tumor is removed by minimally invasive means and lung function is preserved. In contrast, patients with the MIP pattern who underwent lobectomy had only a 12 percent incidence of recurrence over a five-year period.

It currently takes an expert lung pathologist to identify the MIP pattern during an operation. If the surgeon performs lung-sparing surgery in the presence of the MIP pattern, the chance of recurrence is high within the spared lobe of the lung. A lobectomy can reduce this chance of recurrence by 75 percent. If the MIP pattern is not found, the surgeon can confidently perform lung-sparing surgery.

Only a handful of cancer centers in the country

have the expertise needed to identify the MIP pattern during surgery. Patients whose tumors are later found to have the MIP pattern after lung-sparing surgery may require another excision or a full lobectomy to reduce their risk of recurrence.

*Breast Cancer*

## 20% of Women Do Not Believe Tailored Risk Assessments

According to a study, 20 percent of women do not believe their breast cancer risk, despite taking a tailored risk assessment that factors family history and personal habits.

Most of the women who did not believe their risk numbers said they did not feel it took into account their family history of cancer or their personal health habits—though the tool did ask relevant questions about the individual's family and personal history.

The findings, published in Patient Education and Counseling, are part of a larger study looking at how to improve patients' understanding of risk information.

Some 690 women who were at above-average risk of developing breast cancer completed a web-based decision aid that included questions about age, ethnicity, personal history of breast cancer, and number of first-degree relatives who had had breast cancer. The women were then told their five-year risk of developing breast cancer and given information about prevention strategies.

After receiving this information, the women were asked to recall their risk of breast cancer within the next five years. If they answered incorrectly, they were asked why: they forgot, made a rounding error or disagreed with the number. The researchers found that 22 percent of women who misreported their risk said they disagreed with the numbers.

The most common reason women said they disagreed with their risk was that their family history made them either more or less likely to develop breast cancer. Many believed that because an aunt or father had cancer, it increased their risk, while only first-degree female relatives impact a person's breast cancer risk. Others felt a lack of family history meant their cancer risk should be very low.

One-third of women cited a gut instinct that their risk numbers just seemed too high or too low.

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## Circulating Tumor Cells Predict Treatment Resistance In Study Of Metastatic Breast Cancer

A study of an in vitro diagnostic test for women with metastatic breast cancer evaluated the utility of circulating tumor cell measurements in predicting responses to anti-cancer therapies, and assessed patients across various disease subtypes.

The study, conducted in China, demonstrated that enumeration of CTCs before and after initiation of standard anti-cancer therapies can be a useful predictor of progression-free survival and overall survival. The study lead to the approval of the test in China.

The CellSearch system, developed by Janssen Diagnostics, has also obtained FDA 510(k) clearance for use with metastatic breast, colorectal or prostate cancer patients.

The study, published in Annals of Oncology, was conducted in 300 Chinese patients with metastatic breast cancer with an ECOG performance status of 0 to 2 starting a new line of systemic therapy—including any form of endocrine manipulation, cytotoxic chemotherapy or immunotherapy, alone or in combination. CellSearch was used to detect the number of CTCs in 7.5 mL of whole peripheral blood.

The primary objective was to evaluate whether a five CTC cutoff point is predictive of PFS and OS in this patient population. In multivariate Cox regression analyses, the baseline CTC number remained an independent prognostic factor for PFS and OS. Similar results were observed for CTC counts at the first follow-up visit for both PFS and OS.

At baseline, 115 (39.1 percent) patients had a CTC count of more than five. These patients had a significantly shorter median PFS of 6.7 months (95% CI = 4.7 to 7.9) and an OS of 13.2 months (95% CI = 10.6 to 15.9) compared with patients who had less than five CTCs, with a median PFS of 9.0 months (95% CI = 7.3 to 11.3, $p<0.001$) and a median OS of greater than 24.6 months ($p<0.001$).

CTC levels correlated to the sites of metastatic disease, hormone receptor status and human epidermal growth factor receptor-2 status and ECOG performance status.

At first follow-up, patients with a CTC count of less than five (n=178) exhibited a significantly longer median PFS (8.2 vs. 5.9 months; $p=0.012$) and OS (20.1 vs. 12.4 months; $p<0.001$) compared to the 49 patients with more than five CTCs.

At the second CTC follow-up, the 39 (16.7 percent)

patients with more than five CTCs had a significantly shorter median PFS (2.0 months) and OS (9.5 months) than did the 194 patients with a CTC count of less than five (median PFS = 7.6 months, p<0.001; median OS >23.2 months, p<0.001). There were no differences in PFS between those HER-2 positive patients whether or not they received anti-HER-2 treatment at the first follow-up (p=0.622), as well as the second follow-up (p=0.479).

In the subset of triple-negative breast cancer patients, at both the first and second CTC follow-up visits, those with a CTC count of less than five had significantly longer median PFS (p<0.001 and 0.002) and OS (p=0.003 and <0.001) times compared to those with more than five CTCs. For all 294 patients, the median PFS and OS were 7.9 months (95% CI = 6.8 to 8.9 months) and 20.9 months (95% CI = 17.3 to >24.8 months), respectively.

*Melanoma*

## Study Finds Gene Expression Test Predicts Stage I or II Recurrence

Validation data showed that a gene expression profile test is a strong independent predictor for classifying which stage I or II non-metastatic cutaneous melanoma patients will likely recur.

The DecisionDx-Melanoma test predicts metastasis by measuring the expression levels of 31 genes in the patient's tumor and stratifies patients as either low or high risk. To date, the test has analyzed archived tumor samples from more than 400 stage I and II melanoma patients in prospectively designed studies.

The data were presented at the summer academy meeting of the American Academy of Dermatology.

The multi-institutional validation study included archived tumors from 78 stage I and II melanoma patients. Gene expression profiles were measured from formalin-fixed, paraffin-embedded biopsies or wide excisions of primary melanoma tumors.

Kaplan-Meier analysis for five-year metastasis free survival rates were 98 percent for low risk and 37 percent for high risk [P<0.0001], with 85 percent accuracy and 86 percent sensitivity. Cox proportional multi-variate analysis found the test to be independent of Breslow, mitosis and ulceration as well as AJCC stage (p<0.01). These data confirm the results of previous studies demonstrating that the gene expression profile test accurately stratifies metastatic risk in stage I and II melanoma patients.

The test is developed by Castle Biosciences Inc.

## NCI CTEP Approved Trials For the Month of August

The National Cancer Institute Cancer Therapy Evaluation Program approved the following clinical research studies last month. For further information, contact the principal investigator listed.

**Phase I**

9343: A Phase 1 and Pharmacokinetic Study of Dabrafenib (GSK2118436B) in Patients with BRAFV600X Mutations and Renal or Hepatic Dysfunction. Mayo Clinic; Haluska, Paul. (507) 284-2511

S1312: A Phase I Study of Inotuzumab (NSC-772518) in Combination with CVP (Cyclophosphamide, Vincristine, Prednisone) for Patients with Relapsed/ Refractory CD22-Positive Acute Leukemia (Including B-ALL, Mixed Phenotypic Leukemia and Burkitt's Leukemia). Southwest Oncology Group; Advani, Anjali S. (216) 445-9354

**Phase III**

A011106: ALTernate Approaches for Clinical Stage II and III Estrogen Receptor Positive Breast Cancer NeoAdjuvant TrEatment (ALTERNATE) in Postmenopausal Women: A Phase III Study. Cancer and Leukemia Group B; Ma, Cynthia Xiuguang.(314) 362-9383

A031201: A Phase III Trial of Enzalutamide (NSC#766085) Versus Enzalutamide, Abiraterone and Prednisone for Castration Resistant Metastatic Prostate Cancer. Cancer and Leukemia Group B; Morris, Michael J. (646) 422-4469

**Other Phases**

AAML13B4-Q: Epigenetics of Down Syndrome Myeloid Leukemia. Children's Oncology Group; Crispino, John. (312) 503-1504

AOST13B2-Q: Investigating Novel Biomarkers for Pediatric Osteosarcoma. Children's Oncology Group; Yustein, Jason Todd. (713) 798-4450

*FDA News*

# FDA Grants Orphan Designation To E7777 in T-Cell Lymphoma

**FDA granted orphan drug designation** to an investigational compound, **E7777**, developed by Eisai Inc., for cutaneous t-cell lymphoma.

The compound is designed to have an improved purity profile and manufacturing process. It is being studied in a phase III trial.

The Orphan Drug Act allows FDA to grant orphan status to a drug which has the potential for the treatment, diagnosis, or prevention of a rare disease or disorder that affects fewer than 200,000 people in the U.S.

CTCL begins in the white blood cells and attacks the skin. It is one of several types of lymphoma collectively called non-Hodgkin lymphoma.

**FDA granted orphan drug designation** for EPZ-5676 for acute leukemia patients with MLL rearrangements.

EPZ-5676, a small molecule inhibitor of DOT1L, is being developed by Epizyme Inc. for the treatment of acute leukemias in which the MLL gene is rearranged due to a chromosomal translocation. Due to the translocation, DOT1L is recruited to specific locations in the chromosome where it would not normally be present. As a result, DOT1L causes inappropriate methylation at these locations, which results in the increased expression of genes causing leukemia.

In September 2012, Epizyme initiated a Phase 1 clinical trial for EPZ-5676. As of August 2013, this program is in the dose escalation phase and is expected to initiate an expansion phase in the second half of 2013 that will exclusively enroll MLL-r patients.

**FDA approved the Aptima HPV assay** for use on the automated Panther system, both developed by Hologic Inc.

The test is performed with a ThinPrep liquid cytology specimen, which are routinely used for Pap testing, and can be tested before and after it has been processed for cytology testing on the ThinPrep 2000 system.

The mRNA based assay is a nucleic acid amplified test that detects 14 high-risk strains of human papillomavirus associated with cervical cancer and precancerous lesions, and has demonstrated significantly improved specificity with no compromise in disease detection. The addition of the Aptima HPV assay to the Panther system allows low to high-volume laboratories to run multiple tests from a single specimen, on a flexible and automated molecular testing platform.

The Aptima HPV assay has been approved for two uses: to screen women 21 years and older with atypical squamous cells of undetermined significance to determine the need for referral to colposcopy; and to use adjunctively with cervical cytology to screen women 30 years and older to assess the presence or absence of high-risk HPV types.

**GlaxoSmithKline announced that it will discontinue** the manufacture and sale of the Bexxar therapeutic regimen February 20, 2014.

The Bexxar regimen (tositumomab and iodine I-131 tositumomab) is approved in the U.S. and Canada for the treatment of patients with CD20- positive relapsed or refractory, low grade, follicular, or transformed non-Hodgkin lymphoma who have progressed during or after rituximab therapy, including patients with rituximab-refractory non-Hodgkin lymphoma.

Bexxar was approved for use in the U.S. in 2003 and in Canada in 2005. The use of Bexxar has been extremely limited and is projected to continue to decline, according to GlaxoSmithKline, which says it will continue to provide support services for patients and treatment centers over the next six months.

**Teva Pharmaceutical Industries Ltd. and Perrgio Company** announced the launch of a generic equivalent to temozolomide (Temodar).

The product is indicated for the treatment of adult patients with newly diagnosed glioblastoma multiforme concomitantly with radiotherapy and then as maintenance treatment and refractory anaplastic astrocytoma patients who have experienced disease progression on a drug regimen containing nitrosourea and procarbazine.

Temodar had annual sales of approximately $423 million in the U.S., according to IMS data as of December 31, 2012.