# The Clinical Cancer Letter

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*Metastatic Melanoma*

## Phase III Trial Retrospective Analysis Finds Talimogene Laherparepvec Reduced Tumors

A retrospective analysis of a phase III study found that talimogene laherparepvec reduced the size of injected tumors and non-injected metastatic melanoma tumors that had metastasized to other parts of the body.

The study evaluated talimogene laherparepvec in patients with injectable unresected stage IIIB, IIIC or IV melanoma compared to granulocyte-macrophage colony-stimulating factor. Full results were presented during an oral session at the Society of Surgical Oncology Annual Cancer Symposium in Phoenix.

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*Ovarian Cancer*

## Avastin-Zybrestat Combination Increases Progression-Free Survival in Phase II Trial

A phase II study evaluating Avastin in combination with Zybrestat demonstrated increased progression-free survival in recurrent ovarian cancer.

The study, known as Gynecologic Oncology Group protocol 186I, met its primary endpoint of a statistically significant increase in progression-free survival ($p < 0.05$; HR=0.685) for the combination compared to Avastin alone.

The study is the first and currently only randomized trial to test an antiangiogenic therapeutic agent combined with a vascular disrupting agent, without including any cytotoxic chemotherapy.

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*Non-Small Cell Lung Cancer*

## IDMC Recommends Halting Phase III Trial Of Onartuzumab in MET-Positive NSCLC

An independent data monitoring committee recommended that the phase III METLung study be stopped due to a lack of clinically meaningful efficacy, following an interim analysis.

The study evaluated MetMab (onartuzumab) in combination with Tarceva (erlotinib) in previously treated, advanced non-small cell lung cancer with tumors were identified as MET-positive, compared to Tarceva alone. Overall adverse event rates were generally similar between the two groups. Data will be submitted for presentation at an upcoming medical meeting.

Genentech, onartuzumab's sponsor, is evaluating the implications of the METLung study results across the ongoing clinical program.

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## Retrospective Analysis Finds Tumor Shrinkage in Phase III Immunotherapy Trial

(Continued from page 1)

Talimogene laherparepvec is an investigational oncolytic immunotherapy designed to selectively replicate in tumor tissue and to initiate a systemic anti-tumor immune response. It is also engineered to express GM-CSF, a white blood cell growth factor, which can help to activate the immune system.

Of the 295 patients treated with talimogene laherparepvec, almost 4,000 tumor lesions were tracked for this analysis. Half of these lesions were injected with talimogene laherparepvec at least once, while the rest were not injected, including visceral tumor lesions, such as tumors involving solid organs such as the lungs and liver.

The results showed a 50 percent or greater reduction in tumor size in 64 percent of injected tumors. In addition, one-third of uninjected non-visceral tumors, and 15 percent of visceral tumors were also reduced by at least 50 percent. There were 35 melanoma-related surgeries performed during this trial of which 30 percent successfully removed all residual disease.

The most frequently observed adverse events in the phase III study were fatigue, chills and pyrexia. The most common serious adverse events include disease progression in both groups, and cellulitis and pyrexia in the talimogene laherparepvec group. Serious adverse events occurred in 26 percent of talimogene laherparepvec patients and 13 percent of GM-CSF patients. Immune-mediated events were reported infrequently.



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*Palliative Care*

## Study: End-of-Life Chemotherapy Leads to More Deaths in Hospital

Terminal cancer patients who receive chemotherapy in the last months of their lives are less likely to die where they want and are more likely to undergo invasive medical procedures than those who do not receive chemotherapy, according to a study.

The findings underscore a disconnect between the type of care many cancer patients say they want and the kind they receive, and highlight the need for clearer and more balanced discussion of the harms and benefits of palliative chemotherapy at the end of life by doctors, patients and families, the study authors said. The study was published in BMJ.

Whereas 80 percent of patients who did not receive palliative chemotherapy died where they wished, only 68 percent of those whose disease management included palliative chemotherapy died in the place they wanted to. Nearly 66 percent of patients who did not receive palliative chemotherapy died at home, compared to 47 percent of patients who received palliative chemotherapy. Patients who received palliative chemotherapy were much more likely than their counterparts to die in an intensive-care unit, a contrast of 11 to 2 percent.

The reasons for the link may originate in patients' misunderstanding of the purpose and likely consequences of palliative chemotherapy and lack of acknowledgment of their own prognoses, said researchers.

In the study, patients getting palliative chemotherapy were less likely to talk to their oncologists about the care they wanted to receive if they were dying, to complete Do-Not-Resuscitate orders, or to acknowledge they were terminally ill.

With 56 percent of patients receiving palliative chemotherapy in their final months, the findings underscore the potential harms of aggressive use of chemotherapy in dying patients, and the possible need for widespread changes in oncology practice at academic medical centers.

Researchers analyzed data from 386 patients in the federally funded Coping with Cancer study, which followed terminally ill people and their caregivers until after the patients died. During the six-year study, researchers examined how psychosocial factors influenced patients' care. In the month after the patients died, caregivers were asked to rate their loved ones' care, quality of life, and place of death as being where the patient would have wanted to die. The investigators then reviewed patients' medical charts to determine the type of care they actually received in their last week.

Even after the researchers took into account characteristics such as age, marital status, whether a patient had health insurance, their overall physical and mental health, and the treatment they preferred, those who received palliative chemotherapy still underwent more invasive medical procedures in the last week of their lives and in more cases died in ICUs than patients who did not receive palliative chemotherapy. Among those interventions were CPR and mechanical ventilation.

Patients who received palliative chemotherapy were also more likely to be referred to hospice care, which provides comfort care and emotional support, a week or less before they died. Some 54 percent of patients receiving palliative chemotherapy were referred to hospice late, compared to about 37 percent of patients who weren't taking the drugs.

However, researchers said, the results should not be taken to mean that patients should be denied or not offered palliative chemotherapy.

*Ovarian Cancer*

## Avastin-Zybrestat Combination Increases PFS in Phase II Study

(Continued from page 1)

The trial enrolled 107 patients with platinum-sensitive and -resistant recurrent ovarian cancer at 67 clinical sites in the U.S.

Patients were randomized 1:1 into one of two treatment arms: one arm received Avastin (bevacizumab), and the second arm received Avastin plus Zybrestat (fosbretabulin; CA4P). Both therapies were administered intravenously every three weeks and patients were treated until disease progression or until adverse effects prohibited further therapy. Secondary endpoints in the study include safety, objective response rate according to RECIST criteria, and overall survival.

Patients receiving the combination of Zybrestat and Avastin achieved a higher objective response rate, which was not statistically significant. All patients will continue to be followed for overall survival.

Consistent with prior clinical experience with Zybrestat, patients in the combination arm experienced a higher incidence of hypertension compared to the control arm. All cases of hypertension were managed with antihypertensive treatments, as specified in the study protocol.

For this study, Zybrestat is provided to CTEP under a Cooperative Research and Development Agreement with OXiGENE Inc., and bevacizumab is being provided as an investigational agent under a CRADA with Genentech. Bevacizumab is not approved to treat women with ovarian cancer in the U.S.; however, it is approved in other countries for treatment of ovarian cancer.

Zybrestat exerts its antitumor effects through the validated therapeutic mechanism of tumor blood supply deprivation. By selectively affecting and disabling tumor vasculature, Zybrestat reduces the blood supply necessary for tumor growth and survival.

*Metastases*

## Y-90 Radioembolization Stabilizes Liver Metastases in 98.5 Percent Of Breast Cancer Patients in Study

In the largest study of its kind, yttrium-90 radioembolization was found to be safe and provided disease stabilization in 98.5 percent of women with chemotherapy-resistant breast cancer liver metastases.

Researchers reviewed treatment outcomes of 75 women, ages 26–82, whose metastases were too large or too numerous to treat with other therapies.

While chemotherapy is the standard treatmen, many patients will either have progressive liver disease despite multiple different treatment regimens, and others will not tolerate the side effects from toxic agents. According to researchers, patients are considered for Y-90 radioembolization when they have no other treatment options. The research was presented at the Society of Interventional Radiology's 39th Annual Scientific Meeting.

Y-90 radioembolization is a minimally invasive, image-guided therapy where a catheter is inserted and guided into the artery supplying the liver. Micro-beads are administered that emit radiation from inside the tumor, and radiation damage to healthy surrounding tissues is minimized.

In this study, imaging follow-up was available for 69 of the 75 women treated. In all of these women, liver tumors were growing prior to treatment. Following radioembolization, there was disease control in 98.5 percent of the liver tumors, with more than 30 percent reduction in tumor size for 24 women. The treatment had few side effects.

"The value of Y-90 radioembolization in treating patients with non-operative primary liver cancer and metastatic colon cancer has been demonstrated," said Robert Lewandowski, associate professor of radiology at Northwestern University Feinberg School of Medicine. Given the low toxicity and high disease control rates, this therapy is expanding to other secondary hepatic malignancies, he said.

*Prostate Cancer*

## Study: Robotic-Assisted Surgery Offers Better Cancer Control

An observational study found that robotic-assisted surgery for prostate cancer has fewer positive surgical margins than open surgery, and patients who had robotic surgery needed fewer additional cancer treatments afterward.

According to the study, published in the journal European Urology, the higher upfront costs of robotic surgery may be offset by a reduction of additional cancer therapy costs due to better cancer control outcomes.

Researchers compared 5,556 patients who received robotic-assisted radical prostatectomy to 7,878 who received open radical prostatectomy between 2004 and 2009. Data was provided by the Surveillance, Epidemiology, and End Results program.

The researchers compared the two groups by surgical margin status. A positive margin for prostate cancer has been shown to lead to a greater risk of prostate cancer recurrence and death from the disease. Researchers also assessed the use of additional cancer therapy, such as androgen deprivation and radiation, after robotic versus open surgery.

They found that RARP was associated with 5 percent fewer positive surgical margins, 13.6 percent versus 18.3 percent for ORP, and this difference was greater for patients with intermediate- and high-risk prostate cancer. Patients who had robotic surgery also had a one-third reduction in likelihood of using additional cancer therapy within 24 months after robotic surgery compared to open surgery.

*Non-Small Cell Lung Cancer*

## Phase III MetMab Study Stopped After Interim Analysis

(Continued from page 1)

METLung was a double-blind study that randomized 499 patients to receive 150 mg of Tarceva taken daily plus either intravenous 15 mg/kg of onartuzumab every three weeks or intravenous placebo every three weeks. The study also included a companion diagnostic immunohistochemistry test, which was co-developed with Ventana Medical Systems Inc., a member of the Roche Group.

The primary endpoint of the study was overall survival. Secondary endpoints included progression-free survival, objective response rate and safety profile.

Onartuzumab, a monovalent, monoclonal antibody designed to specifically target the MET receptor, is being studied in various cancers. MET is a protein found on the surface of cells and acts as a receptor that binds to Hepatocyte Growth Factor, also known as "Scatter Factor." When HGF binds to MET, it causes MET proteins to form pairs, which triggers a signaling cascade that tells cells to grow, divide and spread to other parts of the body.

## Phase IIb Trial of Vintafolide-Docetaxel Combination Meets Primary Endpoint of Progression-Free Survival

A phase IIb trial of a combination of vintafolide and docetaxel in folate receptor positive recurrent non-small cell lung cancer met its primary endpoint of improved progression-free survival.

The study data showed that risk of disease worsening or death was reduced by 25 percent for patients treated with the vintafolide/docetaxel combination versus docetaxel alone (HR 0.75; p=0.0696, one-sided test). Detailed trial results, including data regarding overall survival, will be presented at an upcoming medical conference.

The trial, named TARGET, was conducted in 199 patients, randomized to one of three arms: vintafolide (EC145/MK-8109) alone, vintafolide/docetaxel combination, or docetaxel alone. Secondary endpoints, including overall response rate and OS, also showed trends in favor of the combination arm. Median OS has been reached for the vintafolide and docetaxel single-agent arms but has not yet been reached in

the combination arm. In addition, the investigational combination regimen showed better activity in patients with adenocarcinoma, a subset analysis pre-specified in the trial design.

TARGET is an international, open-label study designed to evaluate vintafolide in patients with stage IIIb or IV NSCLC with all lesions positive for the folate receptor as determined by the investigational companion imaging agent etarfolatide and who have failed one prior chemotherapy.

Secondary endpoints included the comparison of overall response rate, disease control rate, duration of response, duration of disease control, overall survival of the participants between treatment arms, and the incidence of adverse and serious adverse events.

The safety profile of the combination arm was consistent with those observed with docetaxel alone and vintafolide alone, though a higher rate of hematologic and peripheral neuropathy adverse events were observed in the combination arm. There were no drug-related deaths in the combination arm. Single-agent vintafolide at the schedule evaluated in this study demonstrated less activity than single-agent docetaxel.

Vintafolide is an investigational conjugate of folic acid (vitamin B9) linked to an anti-cancer agent, the potent vinca alkaloid desacetylvinblastine hydrazide (DAVLBH). Since cancer cells generally consume higher levels of folate than normal cells to fuel their growth, some cancer cell types--including ovarian and NSCLC--have high concentrations of the folate receptor on their surface.

Vintafolide is designed to selectively target the folate receptor to deliver the anti-cancer agent to the cancerous tissue. Tumors that have high concentrations of the folate receptor are identified by etarfolatide, a non-invasive imaging diagnostic agent. Intravenous folic acid is used with 99mTc-etarfolatideetarfolatide for the enhancement of image quality.

Vintafolide, etarfolatide and IV folic acid have been granted orphan drug status by the EMA. FDA has also granted orphan drug status to vintafolide and etarfolatide. Further evaluation is ongoing in the global PROCEED phase III clinical trial in folate receptor-positive platinum-resistant ovarian cancer. Vintafolide is sponsored by Endocyte Inc.



## Ceritinib Demonstrates 58% ORR, 7-month PFS in ALK+ NSCLC

Investigational compound LDK378 (ceritinib) achieved an overall response rate of 58 percent and a median progression-free survival of 7 months in adults with advanced anaplastic lymphoma kinase positive non-small cell lung cancer who received 400 mg or higher of LDK378 per day in a phase I single-arm study.

The study evaluated 114 ALK+ NSCLC patients treated with LDK378, including patients who had progressed during or following treatment with commonly prescribed ALK inhibitor crizotinib, and those who had not received prior treatment with an ALK inhibitor.

The study results, published in the New England Journal of Medicine, demonstrated a median PFS of 7.0 months (95% CI; 5.6-9.5 months) in patients with ALK+ NSCLC treated with LDK378 at doses of 400 mg to the maximum tolerated dose of 750 mg per day.

The study also reported an ORR of 59 percent (95% CI; 47-70%) in patients taking LDK378 at 750 mg per day. The responses observed demonstrated LDK378 is active in patients with advanced ALK+ NSCLC, including those who were previously treated with crizotinib, with or without new mutations in the ALK gene.

The most frequent adverse events were nausea, diarrhea, vomiting, fatigue and increased alanine aminotransferase levels. Preliminary data from this publication were first presented at the 2013 American Society of Clinical Oncology annual meeting. The study is ongoing with more data to become available, according to Novartis, the drug's sponsor. The data served as the basis for regulatory application to FDA, with action expected this year.

FDA designated LDK378 a Breakthrough Therapy, which is intended to expedite the development and review of drugs that treat serious or life-threatening conditions.

Several major studies evaluating treatment with LDK378 are being conducted in more than 300 study centers across more than 30 countries. Currently, two phase II trials are fully enrolled and ongoing. In addition, two phase III trials are actively recruiting patients to further evaluate LDK378 in patients with ALK+ NSCLC.

# NCI CTEP-Approved Trials For the Month of March

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**

9591: A Phase I Trial of Single Agent Trametinib (GSK1120212) in Advanced Cancer Patients with Hepatic Dysfunction. University Health Network-Princess Margaret Hospital; Siu, Lillian L. (416) 946-2911

**Phase I/II**

9525: An Open Label, Two-Part, Phase Ib/II Study to Investigate the Safety, Pharmacokinetics, Pharmacodynamics, and Clinical Activity of the MEK Inhibitor Trametinib and the BCL2-Family Inhibitor Navitoclax (ABT-263) in Combination in Subjects with KRAS Mutation-Positive Advanced Solid Tumors. Dana-Farber Cancer Institute; Corcoran, Ryan Bruce. (617) 726-8599

**Phase II**

A091302: Randomized Phase II Study of Sorafenib with or Without Everolimus in Patients with Radioactive Iodine Refractory Hürthle Cell Thyroid Cancer. Alliance for Clinical Trials in Oncology; Sherman, Eric Jeffrey. (646) 888-4234

**Phase II/III**

GOG-0281: A Randomized Phase II/III Study to Assess the Efficacy of Trametinib (GSK 1120212) in Patients with Recurrent or Progressive Low-Grade Serous Ovarian Cancer or Peritoneal Cancer. NRG Oncology Foundation, Inc.; Gershenson, David M. (713) 745-2565

NRG-HN001: Randomized Phase II and Phase III Studies of Individualized Treatment for Nasopharyngeal Carcinoma Based on Biomarker Epstein Barr Virus (EBV) Deoxyribonucleic Acid (DNA). NRG Oncology Foundation, Inc.; Lee, Nancy Y. (212) 639-3341

**Phase III**

A221301: Olanzapine for the Prevention of Chemotherapy Induced Nausea and Vomiting (CINV) in Patients Receiving Highly Emetogenic Chemotherapy (HEC). Alliance for Clinical Trials in Oncology; Navari, Rudolph Modesto. (574) 631-8898

**Pilot Phase**

ARET12P1: A Multi-Institutional Feasibility Study of Intra-Arterial Chemotherapy Given in the Ophthalmic Artery of Children with Retinoblastoma. Children's Oncology Group. Chintagumpala, Murali Mohan. (832) 822-4200

**Other Phases**

AALL13B12-Q: Analysis of Cyclin-Dependent Kinase 5 (Cdk5) Expression and Activity in Childhood ALL. Children's Oncology Group; Pateva, Irina Boyanova. (216) 844-3345

ANBL13B7-Q: Risk Stratification of Stage 4 Neuroblastomas Using a Three-Gene Ratio Score. Children's Oncology Group; Axelson, Hakan. +46462226434

E1608T3: Autoimmune Regulator as a Genetic Determinant of Response to Anti-CTLA4 Antibody Immunotherapy. ECOG-ACRIN Medical Research Foundation, Inc.; Su, Maureen A. (919) 966-0259

NSABP-C08-CS2: Molecular Correlates of Outcomes in Clinical Trials of Colon Cancer. NRG Oncology Foundation, Inc.; Chan, Andrew T. (617) 726-7802

RTOG-TRP-147: Molecular Markers of Anaplastic Gliomas. NRG Oncology Foundation, Inc.; Chakravarti, Arnab. (614) 293-3241

RTOG-TRP-220: Toxicity Profiling: Creating Novel Paradigms to Personalize Cancer Treatment. NRG Oncology Foundation, Inc.; Armstrong, Terri Sue. (713) 500-2044

SWOG-S0800A-SWOG-ICSC: Whole Exome Sequencing of DNA From Pre-Chemotherapy Needle Biopsies of Triple Negative and Inflammatory Breast Cancers Enrolled on the S0800 Trial. SWOG; Pusztai, Lajos. (203) 737-6858

SWOG-S9313C-SWOG-ICSC: Evaluation of BRCAness as Prognostic Marker in Triple-Negative Breast Cancer Patients Treated with Adjuvant Anthracycline-Based Chemotherapy on INT-0137 (SWOG 9313) Trial. SWOG; Sharma, Priyanka. (913) 588-3375

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*Drug Approvals*

# European Commission Approves Subcutaneous Rituximab

**The European Commission approved a subcutaneous formulation of MabThera** (rituximab) for the treatment of patients with follicular lymphoma and diffuse large B-cell lymphoma.

Following the approval of Herceptin SC in September 2013, this is the second European approval for a novel subcutaneous formulation of one of Roche's oncology products using Halozyme's patented Enhanze (recombinant human hyaluronidase) technology.

The European approval was primarily based on data from the pivotal SABRINA study, which was recently published in the Lancet Oncology. Roche has stated that they expect to begin launching MabThera SC in a number of European markets throughout 2014.

**The Japan Ministry of Health, Labor and Welfare granted approval to the Lonsurf combination tablet** T15 and T20 (trifluridine and tipiracil hydrochloride), for the treatment of patients with unresectable advanced or recurrent colorectal cancer, if refractory to standard therapies.

Japan is the first country in the world to grant marketing authorization for Lonsurf, according to Taiho Pharmaceutical Company Ltd., the drugs' sponsor. The approval is based primarily on the results of a randomized, double blind placebo controlled phase II clinical trial conducted in Japan (J003-10040030). Taiho is conducting a global phase III clinical trial, named RECOURSE, on patients with metastatic colorectal cancer refractory to standard chemotherapies.

Lonsurf is a combination drug of trifluridine and tipiracil hydrochloride. Trifluridine is an antineoplastic nucleoside analog, which is incorporated directly into DNA, thereby interfering with the function of DNA. Its blood concentration is maintained via tipiracil hydrochloride.

**The United Kingdom's National Institute for Health and Care Excellence** published its final guidance recommending prescription of Pixuvri (pixantrone) as a cost-effective monotherapy for the treatment of adult patients with relapsed or refractory aggressive B-cell non-Hodgkin lymphoma, including diffuse large B-cell lymphoma.

Publication of the final guidance by NICE follows the final appraisal determination issued in January 2014. The National Health Service is expected to implement the guidance within 60 days.

Pixuvri, sponsored by Cell Therapeutics Inc., is a novel aza-anthracenedione that forms stable DNA adducts and is designed to not bind iron and perpetuate oxygen radical production or form a long-lived hydroxyl metabolite—both of which are the putative mechanisms for anthracycline-induced acute and chronic cardiotoxicity.

**The Microbiology Devices Panel of the FDA Medical Devices Advisory Committee** unanimously recommended that the benefits of the cobas HPV Test as a first-line primary screening tool in women 25 years and older to assess their risk of cervical cancer based on the presence of clinically relevant high-risk HPV DNA outweigh the risks. The panel also voted unanimously that the test is safe and effective for the proposed indication for use.

If approved, the test would become the first and only HPV test indicated as the first-line primary screen of cervical cancer in the U.S.

The cobas HPV Test, developed by Roche, is the only FDA-approved HPV assay that provides specific genotyping information for HPV 16 and 18, the highest-risk types, while simultaneously reporting the 12 other high-risk HPV types as a pooled result, all in one run from one patient sample.

The cobas HPV Test received FDA approval in April 2011 for screening patients age 21 and older with abnormal cervical cytology results and for use adjunctively with normal cervical cytology in women ages 30 and over to assess the presence or absence of high-risk HPV genotypes.

**FDA approved revised prescribing information for the use of Thyrogen** (thyrotropin alfa for injection) to widen the dose range of radioiodine when used for thyroid remnant ablation.

Thyrogen, sponsored by Genzyme, a Sanofi company, is used before radioiodine treatment to enhance uptake of the radiotracer and allows patients to start and continue taking their thyroid hormone replacement therapy, avoiding the untoward effects associated with hypothyroidism. Previously the amount of radioiodine was fixed at 100 mCi—physicians may now select a dose from the range of 30-100 mCi.

The revised prescribing information is based on the results of the two largest prospective studies ever conducted in thyroid cancer. The studies, published in the New England Journal of Medicine in May 2012,

compared ablation success among patients receiving recombinant human thyrotropin and patients undergoing thyroid hormone withdrawal at both low and high doses of radioiodine. In both studies, patients receiving Thyrogen rather than THW had fewer hypothyroid symptoms and preserved quality of life.

Thyrogen is approved as an adjunctive diagnostic tool for serum thyroglobulin testing with or without radioiodine imaging. Thyrogen is also approved in the U.S. and Europe as an adjunctive treatment for radioiodine ablation of thyroid tissue remnants in patients who have undergone a near total or total thyroidectomy for well-differentiated thyroid cancer and who do not have evidence of distant metastatic thyroid cancer.

**Mylan Inc.** and its subsidiary, Mylan Pharmaceuticals Private Limited, launched the world's first **Herceptin biosimilar** in India.

The product, which will be marketed by Mylan under the brand name Hertraz, is a biosimilar to Roche's Herceptin (trastuzumab). Hertraz is indicated for the treatment of HER2-positive metastatic breast cancer and is available in, 440 mg and 150 mg.

Hertraz was approved by the Drug Controller General of India. In support of this approval, Mylan conducted a series of physicochemical and functional assays to demonstrate similarity to the reference brand Herceptin. These analytical methodologies confirmed the high degree of molecular similarity as well as biological activity of Hertraz. In addition, Mylan conducted a multi-center clinical trial to demonstrate comparable safety and efficacy to the reference product.

Mylan has exclusive commercialization rights for biosimilar trastuzumab in the U.S., Canada, Japan, Australia, New Zealand and in the European Union and European Free Trade Association countries.



**Neogenomics Inc.** launched a series of NeoTYPE cancer profiling tests covering 22 different categories of cancer.

The 22 categories of tumors covered in this series of tests are: brain, lung, breast, cervix, colorectal, endometrium, esophagus, stomach, ovary, soft tissue, thyroid, GIST, melanoma, acute myeloid leukemia, myelodysplastic syndrome, AML favorable-risk, chronic lymphocytic leukemia, lymphoma, juvenile myelomonocytic leukemia, myeloproliferative neoplasms, cancer not-otherwise specified, and spliceosomal abnormalities.

The genetic abnormalities are investigated using sequencing, fluorescent in-situ hybridization, methylation analysis, fragment length analysis, and SNP-cytogenetic array technology. Although more than 60 different genes are investigated in all these tumors, only 8-18 genes are investigated per patient or tumor type.

**Clarient** added the THxID-BRAF molecular diagnostic test, developed by **BioMerieux Inc**., to its service offerings.

Clarient, a GE Healthcare Company, will use the test to aid oncologists in selecting metastatic melanoma patients whose tumors carry the BRAF V600E mutation for possible treatment with GlaxoSmithKline's Tafinlar (dabrafenib) as well as in selecting melanoma patients whose tumors carry the BRAF V600E or V600K mutation for possible treatment with Mekinist (trametinib).

The companion diagnostic assay received PMA approval from the FDA in May 2013.

FDA granted clearance to a phase III trial of ThermoDox in hepatocellular carcinoma, named OPTIMA. The study is expected to launch in the first half of this year.

ThermoDox, developed by Celsion Corporation, is a heat-activated liposomal encapsulation of doxorubicin used in combination with radio frequency ablation.

The trial design is based on an analysis of data from the phase III HEAT Study, which demonstrated that treatment with ThermoDox resulted in a 55 percent improvement in overall survival in a substantial number of HCC patients that received an optimized RFA treatment.

The trial is expected to enroll 550 patients globally, at up to 100 sites. The primary endpoint for the trial is overall survival, and the statistical plan calls for two interim efficacy analyses by an independent data monitoring committee.