A new type of immunotherapy, called ASCI (Antigen-Specific Cancer Immunotherapeutics), is being developed as a potential new non-small cell lung cancer treatment.

MAGRIT is an international clinical study looking at MAGE-A3 ASCI in non-small cell lung cancer. One of the antigens in lung cancer is called MAGE-A3. It is found in various cancers, including 30-40% of all non-small cell lung cancers (NSCLC).

The MAGRIT study will involve approximately 2,300 patients. It is open to NSCLC patients with stage 1B, 2 or 3A disease who have had their tumor surgically resected.

The purpose of this clinical trial is to demonstrate the benefit of the immunotherapeutic product GSK1572932A vs placebo in a 2:1 randomization when given to patients with non-small cell lung cancer, after removal of their tumor. A course of 13 injections will be administered over 27 months.

Key Inclusion Criteria:

- Completely resected, pathologically proven stage IB, II or IIIA NSCLC
- Surgical technique for resection of the patient’s tumor is anatomical, involving at least a lobectomy or a sleeve lobectomy
- The patient is free of metastasis
- The patient’s tumor shows expression of MAGE-A3 gene (central testing)
- Mediastinal lymph node sampling is done according to study protocol guidelines
- Administration of adjuvant platinum-based chemotherapy for the treatment of the current NSCLC is allowed between surgery and randomization

For more information or to refer a patient, please call 1-866-379-9646.
Welcome to the first issue of the Florida Hospital Cancer Institute’s (FHCI) medical journal for physicians. Our goal is to keep you informed of key developments in cancer that can help enhance the care you provide to your patients. The FHCI is committed to providing personalized patient care with an expert multidisciplinary team of physicians and support staff utilizing advanced technology in a friendly, supportive environment to achieve optimal patient outcomes.

Multidisciplinary teams of medical and radiation oncologists, surgeons, pathologists and radiologists work together to recommend and implement an optimal, personalized treatment plan. These recommendations are communicated not only to the patient but also to the referring and primary care physicians as well. We work closely with patients’ physicians to ensure patients receive as much treatment and follow up care as possible with their current providers.

Our Clinical Care Coordinators play a vital role in providing this coordinated care. Physician referrals and appointments are arranged and data are collected as the patient and family are guided through the care process. The Breast Care Program to date this year has helped over 700 patients, 158 for breast cancer and 29 for prostate cancer. This and future newsletters will help keep you informed of the various programs and services we provide at FHCI. I hope you find them helpful and let me know if there is anything else we can do.

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**FLORIDA HOSPITAL CANCER INSTITUTE CLINICAL OUTCOMES**

<table>
<thead>
<tr>
<th>TUMOR SITE</th>
<th>INDICATOR</th>
<th>FHCI ACTUAL</th>
<th>NATIONAL RATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain</td>
<td>Overall 5 year survival rate</td>
<td>84%</td>
<td>81%</td>
</tr>
<tr>
<td>Breast</td>
<td>Local recurrence rate within 5 years of surgery</td>
<td>2%</td>
<td>7%</td>
</tr>
<tr>
<td>Urology</td>
<td>Surgical margin positivity rate</td>
<td>10%</td>
<td>34%</td>
</tr>
<tr>
<td>Gyn Onc</td>
<td>Post-OP Length of stay</td>
<td>1 Day</td>
<td>2 Days</td>
</tr>
<tr>
<td>Thoracic</td>
<td>Overall 5 year survival</td>
<td>18%</td>
<td>16.8%</td>
</tr>
</tbody>
</table>

**ABOUT FLORIDA HOSPITAL CANCER INSTITUTE**

The Florida Hospital Cancer Institute is the largest cancer program in Central Florida with 166 dedicated oncology beds at 5 locations and 4 outpatient radiation centers. The Institute is positively impacting clinical outcomes from our care approach that is based on offering clinical trials, tumor site sub-specialization, multi-disciplinary care and care coordination.

For more information, please visit us at www.FloridaHospitalCancer.com.

**CLINICAL RESEARCH**

Since 1989, the Clinical Research Department has provided ongoing access to more than 100 clinical trials at any given time for adult and pediatric patients, including NCI Cooperative Groups (CALGB, COG, CTSU, COG), Duke-in-house, Sarah Cannon Research Institute, pharmaceutical sponsored and UCLA/TORI Network trials. The Florida Hospital Cancer Institute (FHCI) is a flagship member of the Duke Oncology Consortium and is the first site east of the Mississippi to participate in the UCLA/TORI Network.

The FHCI has become the number one hospital in Florida for newly diagnosed patients seeking treatment. Since 1989, more than 2,300 patients who received their care at Florida Hospital Cancer Institute participated in clinical trials. The Clinical Research Department consists of 25 staff members including 11 RN/OCN Coordinators and 30 Physician Investigators, including subspecialties such as bone marrow transplant, gynecologic oncology, neuro-oncology, pediatric oncology and radiation oncology.

In 2006, the Florida Hospital Cancer Institute was one of only 12 community oncology programs in the country to receive honors from the American Society of Clinical Oncology (ASCO) for its commitment to improving care of people with cancer through increased participation in clinical trials.

“With the Clinical Trial Participation Awards we are honoring sites for their exceptional dedication to improving the quality of cancer care by increasing awareness in the community about the value of clinical trial participation,” states Joseph Bailes, MD, Interim Executive Vice President and CEO of ASCO.

**NEW DEVELOPMENTS FOR HEAD AND NECK ONCOLOGY**

Care for our head and neck oncology patients is rapidly improving for a number of reasons. Dr. Jeffrey Baylor, Dr. Mimi Tran, Dr. Brian Spector, Dr. Jeffrey Lehman, and Dr. Henry Ho are all performing the new technique called transoral laser microsurgery. This technique allows removal of tumors through the oral cavity in a conservative fashion, leading to less morbidity and more rapid recovery for the patient. In addition, Dr. Aftab Patni, our neurotologist, is adding to our armamentarium of surgical options for tumors involving the temporal bone. Dr. Brian Spector, with our neurosurgical team, is furthering the options for tumors involving the anterior skull base via a transnasal, transphenoidal approach to tumors in that area. Also, Dr. Henry Ho is involved with transoral/transpalatal approaches to tumors involving the cranioboventral junction. This is also done in coordination with the neurosurgical team at Florida Hospital. Other key specialists on our team include, Dr. David Diamond of radiation oncology and Dr. Paul Baekey of pathology.

We are also streamlining and updating the operating room equipment and personnel and procedures for the benefit of our patients. We are opening the new Otolaryngology Head and Neck Surgery Services Unit at Florida Hospital Winter Park, which will include nursing staff expertise and improved patient care.

For more information or to refer a patient, please call Laurie Amadeo, MSN, ARNP, AOCNP at 407/303-5909.
LUNG CANCER: TIME TO PERSONALIZE TREATMENT

Lung cancer is the leading cause of cancer deaths in the world, greater than 1 million deaths from lung cancer occur each year. Although chemotherapy remains the mainstay of treatment for the majority of patients with advanced non–small-cell lung cancer, targeted therapies have assumed an increasingly important role, particularly in genetically defined subsets of patients. For example, mutations in the epidermal growth factor receptor (EGFR) define a small subset of patients with non–small-cell lung cancer who have sensitivity to EGFR tyrosine kinase inhibitors (TKIs), such as gefitinib (Iressa), or erlotinib (Tarceva). The remarkable success of EGFR TKIs highlights the importance of identifying genotype specific subsets of patients to guide the appropriate selection of targeted therapies.

Another novel approach to treating lung cancer are drugs that prevent formation of new blood vessels (anti-angiogenic drugs), or lead to the destruction of existing ones (vascular disrupting agent, VDAs), leading to deprivation of the tumor from the necessary nutrition and oxygen essential for its growth. These new approaches for individualizing patient treatment have significantly changed the outlook for lung cancer patients. Besides improving the results of treatment, this approach could also result in minimizing side effects and toxicities related to treatment. Clinical trials that utilize these novel agents are currently in progress for lung cancer patients.

The future for lung cancer therapies will likely not be a shotgun approach to all types of tumors but a variety of silver bullets targeting individual tumor types.

Florida Hospital Cancer Institute Oncology Surgical Results

<table>
<thead>
<tr>
<th>TRADITIONAL LOBECTOMY</th>
<th>VATS LOBECTOMY</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>NUMBER</td>
<td></td>
<td></td>
</tr>
<tr>
<td>178</td>
<td>69</td>
<td>247</td>
</tr>
<tr>
<td>MORTALITY RATE</td>
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</tr>
<tr>
<td>1.7</td>
<td>0.0</td>
<td>1.2</td>
</tr>
<tr>
<td>OVERALL LENGTH OF STAY</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8.0</td>
<td>5.0</td>
<td>7.0</td>
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</table>

Source: FHCI Thoracic Cancer Program

ANTI – ANGIOGENIC TARGETED THERAPIES IN MANAGEMENT OF Glioblastoma and OTHER HIGH GRADE GliOMAS

An ever increasing understanding of the molecular pathways involved in signaling transduction, angiogenesis, cell growth and cell invasion has led to the development of a number of targeted agents. Such molecularly targeted agents are under active evaluation, alone and in various combinations, for patients with glioblastoma (GB) and other high grade gliomas (HGG).

Vascular endothelial growth factor pathway – Vascular endothelial growth factor (VEGF) and its three main receptors (VEGFR1, VEGFR2, VEGFR3) are intricately involved in abnormal vasculature formation in GB/HGG and other neoplasms. Antiangiogenic strategies targeting this pathway (some still experimental) include the use of monoclonal antibodies that bind VEGF (e.g. Bevacizumab/Avastin), small molecule inhibitors of the tyrosine kinases (TKs) activated by the VEGF receptors (e.g cediranib/AZD 2171), and inhibitors of protein kinase C, which is an important downstream component of the VEGF cascade (e.g Enzastaurin). These approaches have promising activity in patients with GB/HGG and are under continuing evaluation. The normalization of tumor vasculature induced by these agents can decrease tumor-associated edema and may facilitate the delivery of other cytotoxic agents to the tumor.

Bevacizumab / Avastin is a monoclonal antibody that binds VEGF and prevents its interaction with VEGF receptors on the cell surface. Phase II results indicated that the administration of Bevacizumab, either alone or in combination with irinotecan, may have an unusually high response rate (RR) against recurrent GB/HGG – most studies revealing an initial RR of 55% – 60%. The FDA approved bevacizumab alone for recurrent GB in May 2009. Conversely, there have been some concerns and skepticism in regards to – VEGF therapies promoting an aggressive phenotype in these tumors and potentially paving the path (in some cases) towards increased invasiveness. Overall, Bevacizumab is now a well accepted option for recurrent GB.

Cediranib / Azi 2171 is an oral inhibitor of all of the VEGF receptor TKs, as well as the TKs associated with platelet derived growth factor (PDGF) receptors. In preclinical studies, cediranib decreased tumor vessel permeability and controlled edema despite ongoing tumor growth. These vascular changes required continuation of therapy, and interruption of drug resulted in a recurrence of vascular abnormalities. A phase II study (reported in 2007) demonstrated a partial response by imaging criteria in 9 of the 16 patients treated (56%), and the progression-free survival at six months was 26%. Hypertension due to treatment was observed in 15 patients (93%), 12 of whom required therapy. Additional studies will be required to further delineate the role of cediranib / AZD 2171 in recurrent GB/HGG.

Enzastaurin / LY 317615 is a selective inhibitor of protein kinase C beta, an important component of the VEGF cascade which appears to be the predominant angiogenic factor for GB / HGG. Although a phase II study (reported in 2005) showed promising results, a phase III trial (reported in 2008) in which 266 previously treated patients with recurrent GB/HGG were randomly assigned to either enzastaurin or lomustine/CCNU, showed statistically nonsignificant differences in the objective response rate, progression-free survival (PFS), and overall survival all were inferior with enzastaurin compared to lomustine/CCNU (at the interim analysis).

In summary, molecularly targeted therapies directly/indirectly engaging VEGF and its downstream pathways likely have a future positive in treating GB/HGG and other neoplasms. Experimental therapeutics will be the main defining entity of the utility of these agents. Other agents tested/under investigation that have a bearing directly/indirectly on the angiogenic pathways in GB/HGG are Imatinib (Gleevec), Sorafenib (Nexavar, BAY 43-9006), Sunitinib (Sutent, SU 11248), Erlotinib (Tarceva), Thalidomide and Celecoxib/Celebrex.

For more information or to refer a patient, please call Denise Cochran, MSN, ARNP-BC at 407/303-7132.
PERIURETHRAL SUSPENSION STITCH DURING ROBOT-ASSISTED LAPAROSCOPIC RADICAL PROSTATECTOMY:
Description of the Technique and Continence Outcomes

Panel VR, Coelho RF, Palmer KJ, Rocco B. Global Robotics Institute • Florida Hospital Celebration Health Celebration, FL 34747, USA; University of Central Florida School of Medicine, Orlando, FL 32826-0116, USA.

BACKGROUND: Several studies have shown that robot-assisted laparoscopic radical prostatectomy (RALP) is feasible, with favorable complication rates and short hospital times. However, the early recovery of urinary continence remains a challenge to be overcome.

OBJECTIVE: We describe our technique of periurethral retropubic suspension stitch during RALP and report its impact on early recovery of urinary continence.

DESIGN, SETTING, AND PARTICIPANTS: We analyze and prospectively 331 consecutive patients who underwent RALP. 94 without the placement of suspension stitch (group 1) and 237 with the application of the suspension stitch (group 2).

SURGICAL PROCEDURE: The only difference between the groups was the placement of the puboperineal stitch after the ligation of the dorsal venous complex (DVC). The periurethral retropubic stitch was placed using a 12-in monofilament polyglyconate suture on a CT-1 needle. The stitch was passed right to left between the urethra and DVC, and then through the peristium on the pubic bone. The stitch was passed again through the DVC, and then through the pubic bone in a figure eight, and then tied.

MEASUREMENTS: Continence rates were assessed with a self-administered validated questionnaire (Expanded Prostate Cancer Index Composite [EPIC]) at 1, 3, 6, and 12 months after the procedure. Continence was defined as the use of no absorbent pads or no leakage of urine.

RESULTS AND LIMITATIONS: In group 1, the continence rate at 1, 3, 6, and 12 mo postoperatively was 33%, 83%, 97%, and 97%, respectively. In group 2, the continence rate was 40%, 92.8%, 97.9%, and 97.9%, respectively. The suspension technique resulted in significantly greater continence rates at 3 mo after RALP (p<0.01). The median/mean interval to recovery of continence was also statistically significantly shorter in the suspension group (median: 6wk; mean: 7.338wk; 95% confidence interval [CI]: 6.387-8.288) compared to the nonsuspension group (median: 7wk; mean: 9.585wk; 95% CI: 7.558-11.612; log rank test, p<0.02).

CONCLUSIONS: The suspension stitch during RALP resulted in a statistically significantly shorter interval to recovery of continence and higher continence rates at 3 mo after the procedure.

For more information or to refer a patient, please call Laura Forteo, RN, BSN at 407/303-2408.

VIPUL PATEL, MD
Florida Hospital Cancer Institute Urologic Cancer Program Director

JAMES KENDRICK, MD
Dr. Kendrick joined FHCI Gynecologic Oncology in July 2009. Dr. Kendrick received his medical degree from the University of Alabama School of Medicine. After earning his degree, he completed a residency in Obstetrics and Gynecology at the University of Alabama Birmingham. Following residency, and before joining FHCI, Dr. Kendrick also completed a three-year fellowship in Gynecologic Oncology at the University of Alabama Birmingham. His clinical interests include robotic surgery and the management of all gynecologic malignancies.

Dr. Kendrick has been widely published in peer-reviewed journals such as Gyn Oncology and Obstetrics and Gynecology. He has authored and co-authored over 45 peer-reviewed articles, publications and abstracts.

ROBOTIC-ASSISTED LAPAROSCOPIC HYSTERECTOMY AND LYMPHADENECTOMY FOR ENDOMETRIAL CANCER: Analysis of Surgical Performance

Robert W. Holloway, Safranx Ahmadi, Sara A. DeNardis, Lorna B. Peterson, Nazan Salzana, Glenn E. Bigby IV, Dirk P. Pikaar, Neil J. Finkler

Florida Hospital Gynecologic Oncology

OBJECTIVES: To provide an objective analysis of surgical performance of robotic-assisted laparoscopic hysterectomy (RALH) with lymphadenectomy for endometrial cancer during the learning phase of the procedure and to assess opportunities for improvement.

METHODS: From July 2006 to March 2008, 100 patients with endometrial cancer underwent RALH with lymphadenectomy using the da Vinci® Robotic Surgical System. Data were analyzed for operative time (OT), estimated blood loss (EBL), length of stay (LOS), intra-operative complications, surgical-pathologic factors, and post-operative complications using an intent-to-treat analysis. A comparison of the data on a quartile (Q) basis was performed for the 100 RALH cases and separately for the 65 cases that had a complete pelvic-and-aortic-lymphadenectomy (PAL).

RESULTS: Age and body mass index (BMI) did not change significantly during the study. More grade 3 tumors were treated in the last 50 cases (22% vs. 10%, p<0.05). Stage III tumors were identified in 18.7% cases in Q2-4 and none in Q1 (p=0.05). The number of patients undergoing complete PAL and the number of aortic lymph nodes (LN) removed per case increased each quarter. There were 4.4% conversions to laparotomy. Delayed vaginal cuff healing decreased from 16% in Q1 to 0% in Q3-4. No case required blood transfusion. Comparing first 10 cases to the last 10 cases, the total LN counts increased from 15 to 21 nodes, aortic LN counts increased from 4.7 to 8.0, and the OT decreased from 203 to 160 min. Inter-surgeon analysis revealed an improvement in the total LN yields from 1st 50 to 2nd 50 cases for each surgeon.

CONCLUSIONS: Operative times decreased and aortic dissections improved with increasing LN counts during the first 100 cases of RALH. Furthermore, patient safety and improvement in surgical performance was demonstrated.