The Link

CLINICAL TRIALS NEWSLETTER

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Through clinical research, the new therapies of tomorrow move ever closer to today.

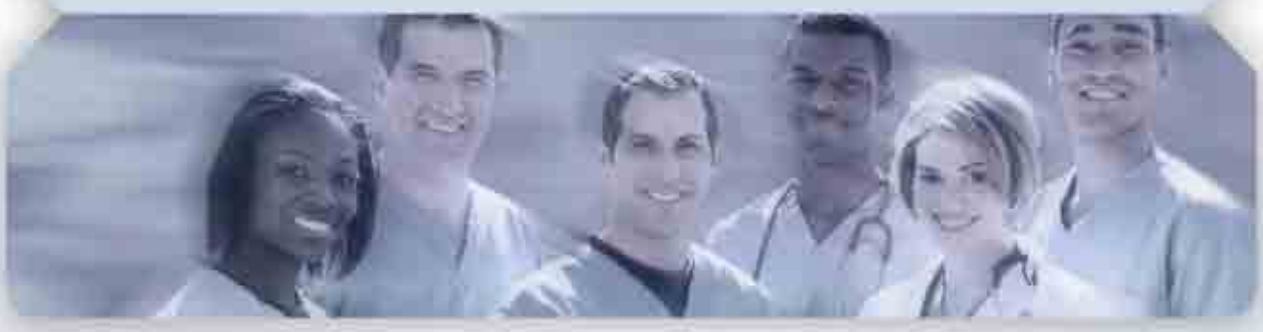
The University of Florida Shands Cancer Center stands at the forefront of an exciting time in scientific discovery that will ultimately have an incredible impact on patient lives. Our physicians, scientists, staff and technicians both in Gainesville and Jacksonville are teamed up and dedicated to partnering with our colleagues in the community to help cancer patients across the State and the Southeast.

Our optimism for future advances in cancer research has been strengthened by the unparalleled commitment of the University of Florida and Shands Healthcare. We have recruited more than sixty national cancer researchers throughout the past four years. A new cancer research building, providing 200,000 square feet of new research space, will open in the spring of 2006. The fifth proton beam therapy facility in the United States will open July 2006 on UF's Jacksonville campus. Renovations are underway at both campuses that will provide patients and their families with a more accessible and pleasant clinical care environment. Finally, a 200-bed cancer hospital on UF's Gainesville campus, that will consolidate all inpatient and outpatient cancer services, is scheduled to open mid-2009. The UF Shands Cancer Center is firmly committed to being at the forefront of defining the new cancer therapies of tomorrow, while bringing these new discoveries to the citizens of Florida and beyond.

This is the inaugural issue of *The Link*, our clinical trials newsletter. This and each subsequent newsletter will highlight some of the exciting and innovative clinical trials underway at our Center. The goal is to alert clinicians of investigative studies that may be of interest or benefit to practitioners and their patients. In this first issue, the focus is on clinical trials for patients with hematologic malignancies, specifically myleodysplastic syndrome (MDS), leukemia, lymphoma and multiple myeloma. A complete listing of all of our clinical trials can be obtained by calling 1-888-254-7581 or consulting the Center's Web site at ufscc.ufl.edu.

John R. Wingard, M.D.
Deputy Director, Gainesville

University of Florida
Shands Cancer Center



Current Clinical Trials
Hematologic Malignancies

Targeted therapy brings new hope for researchers and patients with hematologic malignancies

While the new cytotoxic agents rightfully continue to be tested in the clinics, there is no doubt that we have entered the era of target-specific antineoplastic compounds. It is a great hope that these drugs, either alone or in combination, will be able to change the natural history of the disease and offer patients with diseases, such as MDS, CML or CLL, a chance of sustained benefit.

The researchers at the University of Florida Shands Cancer Center join the world-wide effort in developing new therapeutic strategies for patients with hematologic malignancies, incorporating new, rationally designed, target-specific drugs.

For more information 1-888-254-7581

Randomized Multicenter Trial of Oral SCIO-469 in Patients with Myelodysplastic Syndromes (MDS).

MDS is a clonal disorder of hematopoietic stem cells characterized by ineffective hematopoiesis and eventual transformation into rapidly fatal acute leukemia. The conventional therapeutic agents have never shown much effectiveness in treatment of MDS, and the patients were generally treated with supportive care. The progressive unraveling of the array of pathophysiologic pathways in MDS over the past several years has led to identification of new molecular treatment targets and development of a number of novel, target-specific therapeutic agents, such as inhibitors of farnesyl transferases (Ras inhibitors) and receptor tyrosine kinases, angiogenesis inhibitors and others.

Our center is participating in a large multicenter study of an oral drug SCIO-469, designed to target a p38 Mitogen Activated Protein Kinase (MAPK). MAPK is an enzyme regulating an overproduction of proinflammatory cytokines (IFN-á, -β and –γ, TGF-β, TNF-á, IL-1β), thought responsible for increased apoptosis in patients with early stages of MDS. We are particularly excited about this study since for the first time we have a well tolerated oral drug designed to prevent progression of the disease rather than treatment of late complications. Participation in this trial offers a perfect opportunity for patients with low/intermediate-1 risk, who feel strongly about doing something about their disease before it becomes too late.

New Promising Bcr-Abl Tyrosine Kinase Inhibitor to Treat Imatinib Mesylate (Gleevec) Resistant Chronic Myeloid Leukemia (CML) and Ph(+)ALL

Despite the great success achieved with imatinib mesylate in CML, a small but significant number of patients treated with this agent fail to respond, develop resistance or become intolerant to imatinib. Some of the known mechanisms of resistance are Bcr-Abl-dependent (i.e., mutations of the Bcr-Abl sequence, amplification or overexpression of Bcr-Abl or its protein product), but others are independent of Bcr-Abl. One example of the latter is the overexpression of Src kinases that has been reported in some patients who develop resistance to imatinib. Thus, there is considerable interest in developing more powerful Bcr-Abl kinase inhibitors or dual Bcr-Abl and Src kinase inhibitors, such as BMS-354825.

The results of initial trials of BMS-354825 in patients with CML resistant to imatinib are extremely encouraging. The drug appears to have an excellent toxicity profile with very few extramedullary toxicities. The two phase III clinical trials of BMS-354825 for patients with CML in chronic, accelerated or blast phase, as well as patients with Ph(+)ALL are currently open at our center. The eligibility criteria are standard and require failure on imatinib therapy (resistance or toxicity).

Acute Myeloid Leukemia

1. Newly Diagnosed AML - Non-M3
   A. Decitabine induction vs. standard induction (Age ≥ 60)
   B. Daunorubicin dose-intensification in induction and autologous transplant dose intensification +/- mylotarg in consolidation (Age < 60)
2. Newly Diagnosed AML - M3
   A. Arsenic trioxide-based consolidation therapy with state of the art quantitative PCR for early prediction and detection of relapse (Age 5-75)
3. Newly Diagnosed SECONDARY AML
   A. Amonafide (novel topo-II inhibitor) + HiDAC for induction (Age ≥ 18)
4. AML in Remission
   A. Tipifarnib (Farnesyl transferase inhibitor R11577) in patients with at least CR2 or CR1 after primary induction failure (Age ≥ 18)
5. Salvage Therapy for AML
   A. Cloretazine, a novel alkylating agent, in combination with HiDAC for AML in 1st relapse with a CR1 of ≥ 3 months (Age ≥ 18)

Acute Lymphoblastic Leukemia

1. Newly Diagnosed ALL
   A. Three-way comparison of autologous transplant, allogeneic transplant and conventional consolidation/maintenance (Age 15-65)
2. Ph+ ALL
   A. BMS-354825 for patients that are resistant or intolerant to Gleevac (Age ≥ 18)
3. Relapsed/Refractory B-cell ALL
   A. Open-label, repeat-dose study of Foredesine HCl (BCX-1777) infusion (Age ≥ 18)
   **opening Jan 2006*
4. Relapsed T-cell ALL
   A. Open-label, repeat-dose study of Foredesine HCl (BCX-1777) infusion (All ages)

Chronic Myelogenous Leukemia

1. Chronic Phase CML
   A. BMS-354825 for CML patients that are resistant or intolerant to Gleevec (Age ≥ 18)
2. Accelerated/Blast Phase CML
   A. BMS-354825 for CML patients that are resistant or intolerant to Gleevec (Ages ≥ 18)

Myelodysplastic Syndrome (MDS)

1. Low/Intermediate-1 Risk MDS
   A. P38 MAP kinase inhibitor (Age ≥ 18)

Multiple Myeloma

1. Newly Diagnosed MM
   A. CC - 5013 plus dexamethasone (Age ≥ 18)
   B. Auto/auto +/- thal/dex maintenance vs. auto/allo non-myeloablative transplant (Age ≤ 70)

Lymphoma

1. Recurrent Follicular NHL
   A. Auto vs. allo non-myeloablative transplant (Age ≤ 75)
2. Persistent/Relapsed Diffuse Large B-cell NHL
   A. Bexxar/BEAM vs. Rituxan/BEAM as conditioning for autologous transplant (Age 18-80)
3. Relapsed NHL
   A. Bryostatin-1 plus Vincristine for relapsed low or intermediate grade NHL with relapse after stem cell transplant (Age ≥ 18)

On the Web at ufscc.ufl.edu

The UF Shands Cancer Center is proud to announce two recent additions to its Web site: the Healthcare Professional Section and the Clinical Trials Section.

The *Healthcare Professional Section* can be accessed directly at ufscc.ufl.edu/professional and includes information and resources that will be especially helpful to those involved in clinical care.

The *Clinical Trials Section* provides an interactive clinical trial matching and referral service that is confidential and free of charge. This service provides patients and physicians an easy and efficient way of determining available trials that are appropriate for enrollment. This service can also be accessed by calling 1-888-254-7581.

Please call
1-888-254-7581

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University of Florida
Shands Cancer Center
PO Box 100232
Gainesville FL 32610

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