THE TOOLS

Approved Drugs

■ **Avastin™** (bevacizumab) (Genentech, Inc., South San Francisco, Calif.) has been approved by the FDA for use in combination with intravenous 5-fluorouracil-based chemotherapy as a treatment for patients with first-line—or previously untreated—metastatic cancer of the colon or rectum.

Patients who received IFL (irinotecan, 5-fluorouracil, and leucovorin) plus bevacizumab survived a median of 20.3 months while those on IFL plus placebo had a median survival of 15.6 months. Cancer did not progress for a median of 10.6 months in the bevacizumab group compared to 6.2 months in the other group. Tumors shrank by at least half in 45 percent of the patients who received bevacizumab versus 35 percent in the other group.

Avastin is the first FDA-approved therapy designed to inhibit angiogenesis, by targeting a protein called vascular endothelial growth factor (VEGF).

Drugs in the Pipeline

■ The FDA has granted orphan drug status to **BCX-1777** (BioCryst Pharmaceuticals, Inc. of Birmingham, Ala.), a purine nucleoside phosphorylase (PNP) inhibitor that is in clinical development for treatment of T-cell non-Hodgkin's lymphoma, which includes cutaneous T-cell lymphoma.

BCX-1777, which functions by blocking the T-cell's DNA synthesis machinery, is currently in four Phase I clinical trials at nine leading U.S. cancer centers. BioCryst plans to initiate Phase II clinical trials for BCX-1777 in patients with cutaneous T-cell lymphoma and T-cell leukemia during 2004.

■ Vion Pharmaceuticals, Inc., (New Haven, Conn.) has received fast track designation from the FDA for **CLORETAZINE™** (VNP40101M), a unique sulfonyl hydrazine DNA alkylating agent, for use in relapsed or refractory acute myeloid leukemia (AML). Many patients with AML respond favorably to initial chemotherapy, but in most the disease recurs and ultimately becomes resistant to additional treatment.

■ The FDA has accepted the new drug application (NDA) for **Genasense™** (oblimersen sodium) (Genta, Inc., Berkeley Heights, N.J.), a systemic antisense therapy for cancer. The NDA proposes the use of Genasense in combination with dacarbazine for the treatment of patients with advanced melanoma who have not previously received chemotherapy. In addition, the FDA granted priority review status to the application, which targets an agency action on or before June 8, 2004.

■ Allos Therapeutics, Inc., (Westminster, Colo.) announced that the FDA's Division of Oncology Drug Products has accepted for review the company's NDA seeking approval to market **RSR13** (efaproxiral) as an adjunct to whole brain radiation therapy for the treatment of brain metastases in patients with breast cancer. RSR13 is a synthetic small molecule that has the potential to sensitize hypoxic (oxygen deprived) tumor tissues and enhance the efficacy of standard radiation therapy.

The FDA also designated the NDA for "priority" review, meaning the agency will take action on the NDA filing within six months from the submission date, or by June 2004.

■ The FDA has accepted for filing and granted Priority Review classification for Pharmion Corporation's (Boulder, Colo.) NDA for **Vidaza™** (azacitidine for injectable suspension) for the treatment of myelodysplastic syndromes (MDS).

■ American Pharmaceutical Partners, Inc., (Schaumburg, Ill.) and American BioScience, Inc., have filed a new drug application (NDA) to the FDA for **Abraxane™** for the treatment of metastatic breast cancer. Using proprietary nanoparticle technology, Abraxane combines the active drug paclitaxel with a natural protein called albumin into a nanoparticle 1/100th the size of a red blood cell, avoiding the need for any solvent. Abraxane is the first solvent-free nanoparticle albumin-bound chemotherapeutic, and may potentially exploit an inherent pathway for albumin receptor-mediated transport of drugs across endothelial cell walls of tumor neovasculature.

The filing of the NDA is based upon supportive Phase I and II clinical trials of Abraxane and a pivotal randomized controlled Phase III trial that compared the safety and efficacy of 260 mg/m^2 of Abraxane to

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FAST FACTS

How Americans Feel About the Medicare Prescription Drug, Improvement, and Modernization Act (MMA) of 2003

Reaction	Reaction Dec. 2003	Reaction Feb. 2004
I am very pleased that it passed	10%	9%
I am somewhat pleased that it passed	10%	12%
I am somewhat disappointed that it passed	8%	9%
I am very disappointed that it passed	18%	16%
Don't know	12%	12%
Don't know enough about it to have an opinion	42%	43%

Note: Percentages may not add up exactly due to rounding
Source: The Wall Street Journal Online/Harris Interactive Health-Care Poll available at: *www.harrisinteractive.com.*

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175 mg/m^2 of Taxol® administered every three weeks in 460 patients with metastatic breast cancer.

The Phase III trial demonstrated that Abraxane resulted in an almost doubling of the response rate and a prolongation of time to tumor progression in first- and second-line patients with metastatic breast cancer. In addition, the study confirmed that Abraxane could be administered safely over 30 minutes without the need for steroid premedication.

■ The FDA has granted orphan drug designation to Exelixis, Inc., (South San Francisco, Calif.) for **XL119** (DEAE rebeccamycin), an experimental treatment for bile duct tumors. The company anticipates initiating a pivotal Phase III clinical trial for XL119 for this indication in 2004.

In related activity, Exelixis has submitted an investigational new drug (IND) application for **XL647**, a propriety novel anticancer compound. XL647 demonstrates potent inhibition in vitro against multiple receptor tyrosine kinases (RTKs) that are implicated in tumor proliferation and vascularization (angiogenesis). Pending clearance from the FDA, Exelixis intends to initiate a Phase I clinical trial in the second quarter of 2004.

■ Cell Therapeutics, Inc., (Seattle, Wash.) has completed the FDA's Special Protocol Assessment review process for a randomized Phase III trial of **Pixantrone** in the treatment of relapsed, aggressive non-Hodgkin's lymphoma (NHL). The trial will examine the complete response rate, time to tumor progression, and overall survival of patients with aggressive NHL who have failed front-line and at least one second-line multi-agent chemotherapy regimen. Patients will be randomized to receive either Pixantrone or another currently used, single-agent drug of the physician's choice.

| On the Internet |

■ ***PubMed***
Did you know that PubMED's "Cubby" feature allows you to store search strategies and update your searches? If you log onto PubMed at *www.nlm.nih.gov/* and then click on Medicine/PubMed on PubMed's homepage, you will find the "Cubby" button on the lefthand sidebar under "PubMED Services." A user-friendly Cubby tutorial with audio/visual instructions will explain how to use the "Cubby" feature.

■ ***www.AccessWatch.org*** is a web site that allows cancer patients, family members, caregivers, and other concerned citizens to document and describe the impact that the Medicare Prescription Drug, Improvement, and Modernization, Act (MMA) is having on cancer care. Specifically, Access Watch will track and analyze information concerning:

- Treatment site closures
- Diminished access of Medicare beneficiaries to cancer caregivers
- Delays in treatment and increased costs associated with the referral of patients from the community setting to hospitals
- A reduction in community cancer practice clinical research capacity
- A reduction of Medicare beneficiaries' access to the latest, most effective therapies
- The effect that these reductions have on the ability of physician practices to provide care to the indigent population.

This web site was launched by the Global Access Project in response to the congressional request to assess the implications of MMA on cancer care. The web site will serve as a national clearinghouse to collect data so that Congress, the Administration and other key decision-makers can assess the impact of recent Medicare reimbursement changes on community cancer care.

| New Products |

■ Nucletron B.V. (Veenendaal, The Netherlands) received 510(k) clearance from the FDA for **Simulix EVOLUTION™**, a new digital simulator system designed for integrated planning, verification, and simulation of radiation therapy. The product is available as a complete system, as well as an upgrade for existing Simulix systems and is already in clinical use in various clinics in Europe.

■ The FDA has granted marketing to **Ariol™ HerSight™ application** (Applied Imaging Corp., Santa Clara, Calif.) to assist in detecting over expression of the HER2 protein in breast cancer patients. When used in conjunction with the DAKO Hercep Test®, Ariol HerSight, is now indicated for use in assessing breast cancer patients for whom Herceptin therapy is being considered. Special testing is required to identify those women who are HER2-positive and candidates for treatment with Herceptin.

■ Beckman Coulter, Inc. (Fullerton, Calif.) is now marketing its new FDA-approved **GI Monitor**, a test that aids in the management of pancreatic cancer. The FDA-approved Access® GI Monitor measures levels of cancer antigen (CA) 19-9 levels in human serum and plasma.

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