

Liver Cancer

Research Update 2013

National Leadership

Medical Director of the Liver, Renal and Retinoblastoma programs, Dr. James Geller, leads several local, national and international targeted initiatives in liver tumors.

Dr. Geller, Dr. Gregory Tiao of Pediatric Surgery, and Dr. Alexander Towbin of Pediatric Radiology are active members of the Children's Oncology Group (COG) Liver Tumor Committee where they lead in their respective disciplines. Dr. Tiao and Dr. Towbin are currently key members of the national front-line study of pediatric hepatoblastoma.

Liver cancer research at CBDi includes an international collaboration involving SIOPEL –the International Society of Pediatric Liver Oncology, and JPLT – the Japanese Liver Tumor Group, and the Children's Oncology Group. Dr. Geller and Dr. Tiao represent COG in this collaboration which is developing the first multi-cooperative group, world-wide, comprehensive pediatric study of hepatoblastoma and hepatocellular carcinoma.

Dr. Geller also contributes to the COG liver tumor committee in novel therapy initiatives both through piloted programs locally at CCHMC as well as through Phase I therapeutic agent development.

Research Highlights

Tumor biological characteristics and molecular target identification

The CCHMC team, building on the generosity of our patients and their families, have amassed a liver tumor bank including dozens of pediatric liver cancer samples. Such samples are being used to identify the expression patterns of various targetable proteins, guiding us in the development and providing rationale for new therapies. One target of specific interest is c-MET, the receptor for 'hepatocyte growth factor', expressed at high levels



CBDi Research extends from laboratory studies to improved treatment

on most if not all hepatoblastomas. Liver cancers also express the DR5 receptor, a known target of the TNF Apoptosis Inducing Ligand (TRAIL) antibodies such as lexatumumab.

Novel therapeutics

Dr. Geller is Chair of the National COG Phase I study of the c-MET inhibitor, tivantinib. C-MET is known to be involved in tumor formation and spread, and is specifically overexpressed and overactive in pediatric renal and liver tumors.

CCHMC investigators recently published the Phase 1 study and clinic effects of lexatumumab in hepatoblastoma, an agent targeting 'death receptors' on liver cancers.

CCHMC investigators have taken lead in the development of the JX-594 oncolytic virus in Phase I development. JX-594 is currently in Phase 2-3 investigation in adult study of hepatocellular carcinoma. A collaboration among interventional radiology (Dr. Kamlesh Kukreja, Dr. Ross Ristagno) and oncology (Dr. Geller) has advanced the use of locally directed therapy to treat advanced unresectable liver cancer that are not amenable to liver transplantation with novel



radioactive bead-based therapy with yttrium 90 (Y90) via a technique called ‘radioembolization’.

Genetics

All patients with hepatoblastoma at CCHMC are offered genetic counseling and testing for possibly underlying predisposition including familial adenomatous polyposis (FAP). We have found that as many as 10% of infants and children with hepatoblastoma, despite no suggestive family history, may in fact have FAP with hepatoblastoma being the presenting feature. The clinical-pathological correlates pertinent to multifocal hepatoblastoma associated with FAP, advancing insight into tumor development in such patients, is a focus of Dr. Anita Gupta (pathology) and team.

Tumor marker standardization in post-transplant patients

The liver tumor team takes an individualized approach to the management of each patient with liver cancer before and after surgery, whether surgery is conventional or transplantation. Factors considered in designing patient treatment plans include tumor response and evidence of disease resistance (tumor marker patterns, imaging response, and tumor necrosis (tumor kill) noted at pathology review) as well as an individual’s tolerance to therapy (hearing status, kidney function, other co-morbidities). Novel tumor markers beyond alpha-fetoprotein are being sought to help us understand whether we can better define when ‘minimal residual disease’ has cleared, enabling optimized titration of the amount of chemotherapy given.

Radiographic correlations to therapy

The radiology department of CCHMC, in collaboration with members of the liver tumor team, have advanced ‘Eovist’ (gadoxetate disodium) Magnetic Resonance Imaging for all patients with or suspected to have liver tumors, as the eovist contrast agent enhances the ability to detect multifocal disease and helps delineate the margins where tumor meets normal tissue, which aids in monitoring therapy response and surgical planning. Our imaging protocols have been exported to other radiology departments throughout the country. A part of the research aspects of eovist imaging have been supported by Bayer Pharmaceuticals.

Clinical therapy correlations and outcomes

In addition, investigators at CCHMC including Dr. Greg Tiao, Dr. James Geller, and Dr. Alexander Towbin (radiology) are leading their respective disciplines on behalf of the COG in developing the first multi-cooperative group global study (COG, SIOPEL, JPLT) of pediatric liver cancer to include infants, children, and adolescents with hepatoblastoma and hepatocellular carcinoma.

Division of Oncology
Cincinnati Children's Hospital
3333 Burnet Avenue, MLC 7015
Cincinnati, OH 45229

cancer@cchmc.org
www.cincinnatichildrens.org/cancer