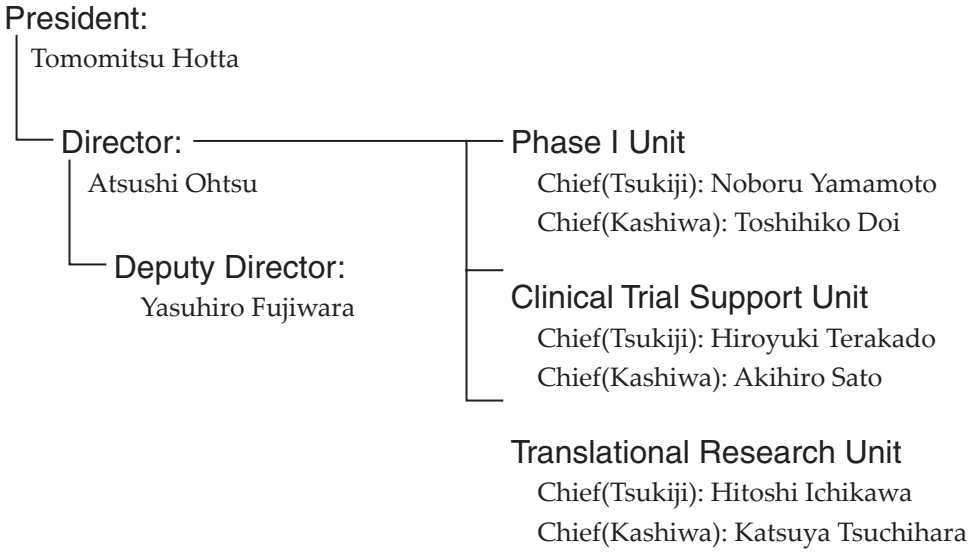
Exploratory Oncology Research & Clinical Trial Center

Preface

In 2011, our National Cancer Center was selected as one of the five designated centers for early/exploratory clinical trial. With a budget support from the Japanese Ministry of Health, Labour and Welfare (MHLW), we organized "the Exploratory Oncology Research and Clinical Trial Center" (NCC-EPOC) through the Kashiwa and Tsukiji campuses consisting of a phase I unit in each campus, central/data center functions for clinical trials, and a translational research (TR) unit. There are three missions of the NCC-EPOC: to conduct first-in-human (FIH) trials, investigator-initiated trials (IIT) with unapproved agents, and TRs during early clinical studies. To date, 10 sponsor-initiated FIH trials have already been conducted in total at both campuses. We have initiated one IIT with an unapproved agent, TAS-102, which was originally developed in Japan and has already completed its accrual in collaboration with 6 major cancer centers. Additional 8 IITs are being planned of which 5-6 studies will start in early 2013 including new agent/vaccines originally developed in the Research Center for Innovative Oncology. We have started a nation-wide screening program for the RET fusion gene, which was newly discovered in the Research Institute of our center, in patients with non-small cell lung cancer (NSCLC), for accrual to a phase II IIT with a RET inhibitor. This study is the first trial for RET positive NSCLC with a large screening program in the world. There are several new seeds from academia in Japan currently being planned for FIH or IIT under discussion with the regulatory authorities and two international studies. TR projects with whole exon sequencing in some cancers are underway to establish molecular epidemiologic data in Japanese patients and a cancer encyclopedia. A genome-guided individualized therapy system in collaboration with Hospital East named the ABC study has also been started, which will be followed by other collaborating institutions. These efforts will contribute to the activation of early clinical trials on new agents and to the organization of an active academic research organization (ARO). The goal of NCC-EPOC is to establish a top innovative ARO in the world based on close alliances between academia-industry-government.

Atsushi Ohtsu, M.D., Ph.D.
Director, Exploratory Oncology Research & Clinical Trial Center

Organization

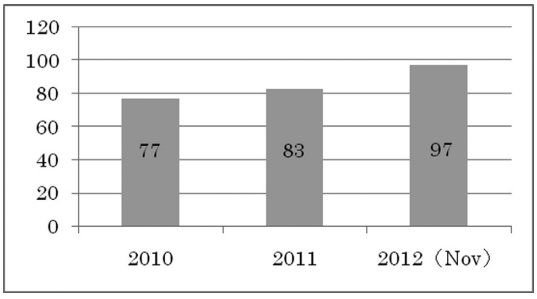


Activities of the Divisions

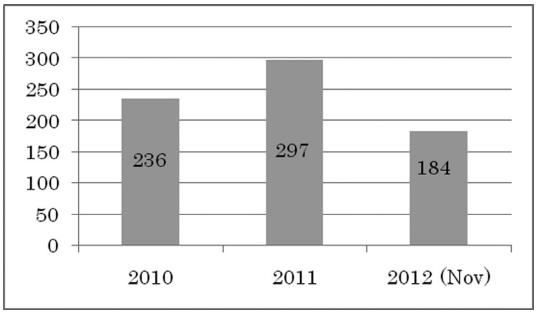
Phase I Unit

Overview of the NCC-EPOC Phase I Unit

The NCC-EPOC Phase I Unit was established in 2012. The NCC-EPOC Phase I Unit consists of two sub-units (NCC & NCCE) which are organized by each Hospital. The goal of both NCC-EPOC Phase I Units is to perform initial clinical evaluation of promising new anti-cancer compounds emerging from the laboratory. We conducted over 100 Phase 1 trials (including FIH trials) and enrolled over 200 patients. Our Phase I Unit is the largest program in Japan, indeed in Asia, and we contribute to the development of new cancer drugs through early phase trials.



Number of contracted phase I trial



Number of accrual pts in Phase I trial

Phase I Unit

The Phase I Unit, with its firm cooperation with all the divisions, serves as the core of the NCC-EPOC clinical development. The cross-divisional phase I team in each hospital consists mainly of investigators from the NCC/NCCE hospitals. The members are as follows:

In addition to the members as above, many young investigators including staff doctors, residents, senior residents, many paramedical staff as well as researchers join the Phase I Unit. Furthermore, the Clinical Trial Coordinating Office and supporting unit of NCC-EPOC in each hospital back us up to jointly implement registration trials and investigator initiated clinical trials.

On a weekly basis, we share information on the progress of the sponsor-initiated clinical trial and the investigator-initiated clinical trial with those core members.

Facilities

At each hospital, based on many years of achievement, advanced equipment as well as abundant specimens and skillful experts are openly available as follows:

- Clinical Trial Wards
- Outpatient Treatment Center
- Clinical Trial Coordinating Office
- Clinical Laboratory Division
- Pharmacy Division
- Diagnostic Radiology Division
- The Research Institute

	NCCHE	NCCH
Director of Phase I Unit	Toshihiko Doi	Noboru Yamamoto
core member	Takayuki Yoshino	Yasuhide Yamada
	Takashi Kojima	Kenji Tamura
	Kouhei Shitara	Yoshitaka Narita
	Nozomu Fuse	Hideki Ueno
	Kiyotaka Yoshino	Yukio Kobayashi
	Yoichi Naito	Atsushi Makimoto
	Nobuaki Matsubara	Motokiyo Komiyama
	Izumi Ohno	Fumihiko Nakatani
	Shigeki Uemura	Naoya Yamazaki
		Ken Ohashi

Clinical Trial Support Unit

Akihiro Sato, Miki Fukutani, Hiromi Hasegawa, Shogo Nomura, Yasuko Nishikubo, Akiko Nakayama, Yasutaka Watanabe, Yukie Kimura, Hiroyuki Terakado, Tamie Sukigara, Nobuko Ushirozawa, Yushi Nagai, Hiroko Nakahama, Noriko Kobayashi, Miki Ito, Shuuzi Misawa, Harue Ui

Introduction

The support unit of EPOC supports seamlessly from the standpoints of planning, protocol development, project management, data management, monitoring, statistical analysis and CRC support across the entire early clinical trial program. This unit is a multidisciplinary team which consists of a clinical research coordinator (CRC), Data manager, Clinical research associate, Medical writer, biostatistician, and various other specialists.

Routine activities

CTM group
- Project management
- Study management
- Site visit monitoring
- Medical writing

DM group
- Data base and CRF form design
- Data management
- Central monitoring
- System administration

Statistical group
- Study design
- Statistical analysis
- Consultation

CRC group
- Support clinical trials that are conducted in the National Cancer Center

IRB office
- Oversees all IRB activities

Research activities and clinical trials

We supported 5 investigator-initiated IND trials using unapproved anti-cancer drugs and 8 non-IND trials using unapproved drugs and medical devices in 2012. Through these studies an electronic data capturing (EDC) system, clinical data management system, and various standard operating procedures were implemented. The CRC group supported over 100 early clinical trials initiated either by industry or investigators in the National Cancer Center in 2012.

Our research activities are mainly focused on clinical trial methodology, organizing infrastructure, and managing early/exploratory clinical trials. For these purposes, we are developing new EDC system, sampling the source document verification (SDV) method and comprehensive information sharing for safety in these trials.

Translational Research Unit

Katsuya Tsuchihara, Yasuhiro Matsumura, Shingo Matsumoto, Hideki Makinoshima, Sachiyo Mimaki, Atsushi Ochiai, Takeshi Kuwata, Akiko Nagatsuma, Yuka Nakamura, Hitoshi Ichikawa, Tatsuhiro Shibata, Natsuko Hama, Takashi Kohno, Akinobu Hamada, Shuichi Shimma, Fumiaki Koizumi, Yasuo Kodera

Introduction

Basic and translational researchers at the Research Center for Innovative Oncology (Kashiwa Campus) and the Research Institute (Tsukiji Campus) are involved in this Unit, the aim of which is to develop novel anti-cancer therapeutics as well as to prove their concepts. The unit also closely collaborates with intramural and extramural clinical research teams to develop companion diagnostic systems and identify biomarkers contributing to individualized cancer therapy.

Routine activities

Translational Research Conferences have been regularly held in both campuses to discuss the strategic approaches to develop novel clinical trials.

Research activities

Individual cancers harbor a set of genetic aberrations such as mutations and gene fusions, and some of them are expected to become informative biomarkers to predict therapeutic response and minimize adverse drug reaction in molecular targeted therapies. In the Tsukiji campus, as a collaborative work with the Center Hospital and Research Institute, systematic genetic testing using hiagh-throughput sequencer (clinical sequencing) is planned to start in 2013, to identify mutations and fusions of potentially targetable genes. This year, sequencing platform comparison and construction of computational analysis pipelines for rapid detection of genetic aberrations were performed. In the Kashiwa campus, the "Analyses of Biopsy Samples for Cancer Genomics study (ABC study)" was planned and carried out in collaboration with the TR unit and all the oncology departments of the Hospital East. The study verified the feasibility of the clinical sequencing. Biopsy samples from the patients, in whom drug therapies were planned, were collected and genomic DNA samples were analyzed with commercially available amplicon sequencing panels containing known hot-spots of cancer-related genes at the validated clinical testing laboratory. In the first 7 months, more than 100 cases have been enrolled and amplicon sequence starting with 10 ng of genomic DNA was successfully performed. The study will be expanded to verify the utility of being able to direct clinical applications in the near future.