

Gastrointestinal Oncology

Introduction

The Gastrointestinal Oncology Division currently focuses on chemotherapy with or without radiation therapy against gastrointestinal malignancies. We treat many patients practically, and participate in various clinical studies to develop a new or standard treatment prospectively. We also investigate the relationship among clinicopathological features, biological characteristics and clinical outcomes of each treatment for the purpose of developing treatment-oriented diagnosis, stratification or individualization of treatment.

Routine Activities

We participate in many clinical studies. A number of inpatients has been increasing year by year. We indicate outpatient-based chemotherapy for possible candidates including new patients. Thus, more than 25 patients receive chemotherapy everyday. The average hospital stay of patients treated with chemotherapy was 14.4 days. The most appropriate treatments for all patients are determined in case conferences consisting of medical, surgical, radiation oncologists, and diagnostic radiologists, and are initiated after obtaining patients' informed consent.

Clinical Trials and New Developments

1. Esophageal Cancer

In practical management, we started to treat RTOG regimens as definitive CRT for esophageal cancer pts which is standard CRT treatment in world-wide nations. We also tried to control residual esophageal cancer after definitive CRT by surgical resection or endoscopic treatment such as EMR (endoscopic mucosal resection), PDT (photo-dynamic therapy) for the improvement of survival.

As investigational trials, a phase II study of chemo-radiotherapy (CRT) with 5-FU + CDDP + RT for stage II/III esophageal cancer has been completed (JCOG9906). A randomized phase II/III study of CRT with standard 5-FU + CDDP+RT vs low dose 5-FU + CDDP + RT for T4/MYLYM esophageal cancer has been started(JCOG0303).

For stage II/III cases, a phase I study of CRT of RTOG regimen has been started and completed

patient accrual. For pts with metastatic/recurrent esophageal cancer, we started dose finding phase I study of DCF (Docetaxel+CDDP+5FU), which is one of important regimen for head and neck cancer.

A comparative phase III study of surgery vs CRT (5-FU + CDDP + RT) for clinical stage I is also planned as JCOG study on the basis of the results from JCOG 9807. A phase II study of combination of EMR and CRT (5-FU + CDDP + RT) for clinical T1b disease is also planned as JCOG study.

2. Gastric Cancer

A phase III study, 5-FU vs CPT-11 + CDDP vs S-1, in advanced gastric cancer patients (JCOG 9912) is presently ongoing. Also, a phase III study of 5-FU vs MTX+5-FU against patients with peritoneal dissemination (JCOG 0106) is underway. A randomized phase II trial of second line chemotherapy (weekly paclitaxel vs best available 5FU) for patients with peritoneal metastasis will be started in 2005.(JCOG0407)

We have reported the results of varidative study of HER2 expression in gastric cancer using commercial kits for breast cancer on ASCO 2004. (ASCO#4053) According to our result, we are planning to join pivotal international phase III approval trial of Trastuzumab (Herceptin; monoclonal antibody to Her2) for metastatic gastric cancer pts. A phase II trial of new agent "E7070" which was developed by Eisai will be started as second line chemotherapy as company driven trial.

3. Colorectal Cancer

We participated in many industrial trials, especially about new target molecules drugs. As an industrial trial, a phase I study of EMD72000 (humanized monoclonal antibody to EGFR) was started in the end of 2003 and completed in 2004, we will reported on annual meeting of ASCO in 2005.

ABX-EGF (monoclonal humanized antibody to EGFR), PTK787 / ZK 222584 (VEGF tyrosine kinase specific inhibitor), RO4876646 (bevacizumab: anti-monoclonal antibody to VEGFR) are also presently ongoing, these new agents are expected to developing new way to treat in metastatic colorectal cancer.

In investigational trials, a phase I/II study of the combination of intrahepatic arterial infusion of 5-FU and intravenous CPT-11 for the patients with hepatic

metastasis has been initiated in 2003 (JCOG 0208). Also, phase III study of adjuvant chemotherapy (5-FU/LV vs UFT/LV) is now underway (JCOG 0205).

We started FOLFIRI (infusional 5FU/LV and CPT-11) regimen which is one of the standard treatment for metastatic colorectal cancer in practical management.

4. Gastric Lymphoma

A multi-institutional prospective study of stomach preserving treatment including eradication of H. pylori, radiation and chemotherapy against localized gastric lymphoma is underway. Patient accrual has been completed and preliminary results of this study was

reported on annual meeting of ASCO in 2004(ASCO #6527,6559).

Others

A phase II study of STI571 against gastrointestinal stromal tumors (GIST) was completed in 2003 and we reported the results of the study on ASCO 2004 (ASCO #4078). In this year, a phase II study of STI571 as adjuvant chemotherapy for GIST has been started. A phase I study of SU11248 for GIST, new multi-targeting molecule agents, is now underway.

● K.Mera, T.Yano, T.Doii ●

Average Hospital Stay (Days) in GI Oncology Division (1994-2004)

	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004
All cases	35	36.7	23.9	17.8	15.2	16.7	14.2	13.8	12.3	13.3	12.1
	-15	-19	-10	-8	-8	-9	-8	-8	-7	-7	-7
Chemotherapy or Palliation case	44.8	44.4	28.6	19.9	16.8	17.8	15.2	15.1	13.5	15.1	14.4
() : median (days)	-25	-31	-16	-11	-9	-11	-9	-10	-8	-9	-8

Number of Patients in GI Oncology Division (1994-2004)

	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004
Total number of inpatients	369	394	625	737	953	1059	1226	1340	1418	1562	1648
No. of new referrals	181	191	259	313	346	360	439	457	549	645	666
Endoscopic treatment	50	46	66	102	119	91	118	122	150	225	235
Chemotherapy cases	122	141	191	219	223	269	321	335	399	420	431
Esophageal	31	33	56	79	73	106	118	141	174	192	194
Stomach	65	69	78	71	91	77	114	129	135	149	133
Colorectal	26	39	57	69	57	86	89	65	90	79	84

Clinical Study in GI Oncology Division of 2004

Organ	Regimen	Phase	No. of patients
Stomach	5-FUci vs CPT-11+CDDP vs S-1 (JCOG9912)	III	11
	5-FUci vs MTX+5-FU (JCOG0106)	III	7
Esophageal	Standard PF vs Low dose PF (JCOG0303)	II/III	4
	RTOG 50.4Gy (in house)	I	1
	DCF (in house)	I	3
Colorectal	5-FU+LV vs UFT+LV adjuvant (JCOG0205)	III	
	PTK787/ZK 222584 (industry)	I	2
	RO4876646+5-FU/LV	I/II	4
Non specific	EMD72000	I	4
	ABX-EGF	I	3
GIST	SU11248 (industry)	I	2
	STI571 adjuvant	II	1
Total			42
GIST;gastrointestinal stromal tumor,			