

The Gastrointestinal(GI) Oncology Division

Introduction

The Gastrointestinal (GI) Oncology Division currently focuses on chemotherapy with or without radiation therapy to treat GI malignancies, including Head and Neck cancer (HNC). As routine management, standard chemotherapy for these conditions has been performed in many patients. Investigational approaches were evaluated using endoscopic, biological, and molecular analysis to predict clinical outcomes.

Routine Activities

The staff of the division consists of 8 medical oncologists and 11 residents. In 2006, 1702 hospitalized patients (665 of whom were newly diagnosed) were treated at our division. Of these patients, 60 were entered for clinical trials. Outpatient-based chemotherapy for possible candidates was managed passively, and the average hospital stay of patients treated with chemotherapy or palliative therapy was short, at about 20 days. Inter-group meetings with the Surgical/Radiation Oncology Division are held routinely to direct treatment for each or to discuss strategies.

Esophageal Cancer (EC)

More than 200 patients with EC were treated in 2006. A combination of chemo and radiation therapy (CRT) was used with/without salvage approaches (surgery, EMR, PDT, etc.) for EC as definitive treatment. The international standard RTOG regimen (5-FU + CDDP + RT 50.4 Gy with multi-port irradiation) was carried out in over 120 patients with Stage II/III EC in 2004. This year, the JCOG esophageal oncology group has been restructured by merging with the JCOG-GI subgroup. It was decided to cooperate in trials

conducted to establish standard treatments for EC.

JCOG 0508: phase II study of combination endoscopic mucosal resection (EMR) and CRT for stage I EC

JCOG 0502: phase III study of randomizing surgery and CRT for stage I EC

JCOG 0303: phase III study of standard dose vs. low dose CDDP+5-FU+RT for patients with T4 and Stage II EC

DCF (Docetaxel + CDDP + 5-FU) for metastatic/recurrent EC is also planned from the results of the foregoing phase I trial. A phase II trial of weekly paclitaxel for metastatic/recurrent state has been started as a industry-driven trial, and JCOG0604 (phase I/II study of S-1 + CDDP + RT for stage II/III EC) as an investigator-driven registration trial will be held in 2007.

Chemo/radiotherapy are also used to relieve symptoms of EC for far-advanced EC.

Curability/feasibility of PDT as a research trial has been evaluated in 18 patients with loco-regional failure after CRT. Research studies using the array genetic method are also ongoing for predicting the outcome of CRT.

Gastric Cancer (GC)

Several agents (TS-1, CPT-11, Taxan) have led to greater clinical benefits in patients with advanced/metastatic GC. As a Phase III study, 5-FU vs. CPT-11 + CDDP vs. S-1 in advanced gastric cancer patients (JCOG 9912) closed successfully in 2006. The results will be shown at the 2007 ASCO meeting and a standard regimen for metastatic/unresectable GC will be established. For patients with peritoneal dissemination, a phase III study of 5-FU vs. MTX + 5-FU (JCOG 0106) is under way. Recruitment will soon be complete. A randomized

phase II trial of 2nd-line chemotherapy (weekly paclitaxel vs. best available 5FU) is ongoing. (JCOG0407). A phase III industrial trial of Herceptin in combination with capecitabine + CDDP (CP) compared with CP alone in patients with HER2-positive advanced GC has started. This is the first global sponsored study involving the Japanese; however, recruitment (over 40 patients have been registered for the trial) is proceeding very well. SU11248, which is a multi-target kinase inhibitor, has also been subjected to a global phase II trial. An interim analysis will be reported at the 2007 ASCO meeting. Further clinical developments of new drugs will be started in 2007 (bevacizumab, raptinib, RAD001, L-OHP and others).

Colorectal Cancer (CRC)

L-OHP-based treatment (FOLFOX) as well as CPT-based regimens have been routinely used in metastatic/adjuvant/neo-adjuvant treatment. Over 100 patients were successfully treated as outpatients in 2006. The phase II trial of ABX-EGF (fully-humanized antibody to EGFR) is now closed. It showed similar results in the Phase III global trial. Adjuvant/neoadjuvant management in practice has been carried out in cooperation with a surgical group. A phase III study of adjuvant chemotherapy (5-FU/LV vs. UFT/LV) is now complete (JCOG 0205). Bevacizumab (avastin: A), capecitabine (xeloda) combination regimens as key drugs for CRC have been evaluated in feasibility confirmation trials. Bevacizumab is likely to be approved in 2Q/2007. Concerning concurrent global development,

Number of patients in the GI Oncology Division (2006)	
	2006
Total number of inpatients	1702
No. of new referrals	665
Endoscopic treatment	356
Chemotherapy cases	619
Esophageal	224
Stomach	151
Colorectal	126
H&N	98

AVANT, the first international study, is going ahead to evaluate whether the addition of Avastin to chemotherapy as an adjuvant treatment can reduce the risk of recurrence. Enrolment has also begun in Japan.

Head and Neck Cancer (HNC)

The Japan Clinical Oncology Group (JCOG) is planning a multicenter phase II study of concurrent chemoradiotherapy with S-1 and CDDP for locally advanced unresectable head and neck cancer (HNC). Furthermore, we have conducted a phase I trial of combination chemotherapy with docetaxel, cisplatin and S-1 for recurrent and/or metastatic HNC.

Others

Phase II studies of SU11248 and AMG706 for GIST were closed. More phase I trials for GI-specific malignancy were conducted in 2006 than in 2005 (TAS102, SAHA, NK012, etc). A whole series of new drugs is likely to arrive in 2007, including c-met, VEGF-TRAP, TRAP-I, and IGF-RI.

Investigators in the GI Oncology Division have worked especially hard to maintain their leadership in new developments in Japan as well as globally.

● T. Doi ●

Clinical studies at the GI Oncology Division in 2006

Organ	Regimen	Phase	No.
Stomach	5-Fuci vs. MTX+5-FU (JCOG0106)	III	6
	Weekly PTX vs. best available 5FU(JCOG0407)	III	1
	Capecitabine +CDDP+/- Herceptin	III	7
	SU11248	II	2
Colorectal	FOLFOX+AVASTIN	I/II	7
	XELOX+AVASTIN	I/II	12
	C225	II	8
Adjuvant	ABX-EGF	II	8
	S-1+L-OHP	I/II	8
	AVANT(XELOX or FOLFOX+/-AVASTIN)	III	1
Adjuvant	5FU+LV vs. UFT/LV(JCOG0205)	III	6
Adjuvant	AMG706	II	3
GIST	SU11248	I/II	11
H&N/EC	Weekly PTX	II	9
Non-specific	TAS102, RAD001, SAHA, DJ927, NK012, E7070	I	21