

Gastrointestinal Oncology

Introduction

The Gastrointestinal (GI) Oncology Division currently focuses on chemotherapy with or without radiation therapy against gastrointestinal malignancies, and also extends the management of head and neck cancer in this year. We treated many patients practically, and participated in various clinical studies to develop a new or standard treatment prospectively. We conducted many early phase trials to develop and select new active agents for GI&HN malignancies and also investigated 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. 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 or palliative therapy was 18.6 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

The results of a phase II study (JCOG 9708) of chemoradiotherapy (CRT) for stage I disease was reported (ASCO 2003#1147). On the basis of the results from it, a comparative phase III study of surgery vs CRT (5-FU + CDDP + RT) for clinical stage I is scheduled as JCOG study. A phase III study (JCOG0303) of standard dose vs. low dose CRT (5-FU+CDDP+RT) regimens for pts with T4 and stage ‡Wa is now ongoing. To evaluate for new triplet chemotherapy, Phase I study of DCF regimen (Docetaxel+CDDP+5-FU) was now started. Furthermore, for expanding indication of active oral

5FU, we are conducting phase I/II study of S-1+CDDP+RT for patients with stage II/III esophageal cancer as an investigator driven trial. In practical management, we have treated with RTOG schedule (total RT dose 50.4Gy without split) for two years as definitive CRT to stage II/III esophageal cancer pts to reduce CRT toxicity and complications of salvage surgery. We have actively salvaged pts with residual cancer after CRT using surgical resection, endoscopic treatment such as EMR (endoscopic mucosal resection) ,PDT (photo-dynamic therapy). Now, we are evaluating of curability and feasibility of salvage PDT for loco-regional failure after CRT with a phase II study. 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

Enrollment of Phase III study, 5-FU vs CPT-11 + CDDP vs S-1, in advanced gastric cancer patients (JCOG 9912) has been completed, the final results will be shown in 2007. 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 just started (JCOG0407) .According to our results of varidative study of HER2 expression in gastric cancer (ASCO#4053), pivotal international phase III approval trial (ToGA study) of Trastuzumab (Herceptin:,monoclonal antibody to Her2) for metastatic gastric cancer pts, which is our first attending global approval study in gasric cancer is now ongoing. And following new global trials of SU11248 (multi-targeting agents), bevacizumab etc for gastric cancer will be held in 2006. A phase II trial of new agent "E7070" ,which was developed by Eisai has started as second line treatment. New early phase trials of gastric cancer specific agents will be planned and conducted in 2006.

3. Colorectal Cancer

In 2005, chemotherapy for metastatic colorectal cancer has dramatically improved because of approval with infusional 5FU+LV,I-OHP. We have just been able to treat with FOLFOX and FOLFIRI regimen, which have been accepted nation-wide standard schedules for metastatic colorectal cancer. We have

started to confirm the feasibility of FOLFOX4 prospectively in our practical management (162 patients were totally treated with FOLFOX in 2005). Phase I/II study of a combination regimen of oxaliplatin plus S-1, which is most common oral 5FU has been started as an industrial trial. For pts with hepatic metastasis, a phase I/II study of intrahepatic arterial infusion of 5-FU plus intravenous CPT-11 has been active in 2003 (JCOG 0208). Also, phase III study of adjuvant chemotherapy (5-FU/LV vs UFT/LV) is now underway (JCOG 0205). We actively handled industrial development trials of new drugs. A phase I study of EMD72000 (humanized monoclonal antibody to EGFR) was reported (ASCO 2005). Trials of ABX-EGF (humanized monoclonal antibody to EGFR), PTK787 / ZK 222584 (VEGF tyrosine kinase inhibitor) were also completed and RO4876646 (bevacizumab: monoclonal antibody to VEGF) with 5FU/LV are still ongoing. Phase II study of cetuximab (chimeric monoclonal antibody to EGFR) and study of FOLFOX4, XELOX with bevacizumab has been planned for fast approval to catch up with following global development.

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. g of ASCO in 2004 (ASCO #6527,6559).

5. Others

A phase I/II study of SU11248 for GIST, new

multi-targeting molecule agents, is now underway. And several new agents for GI malignancies will be conducted in 2007.

6. Head and Neck cancer (HNC)

We reported the results of a phase I trial of concurrent chemoradiotherapy with S-1 and CDDP in patients with unresectable locally advanced squamous cell carcinoma of the head and neck (SCCHN) at this ASCO meeting (ASCO 2005, abstract 5575). The CR rate was very promising, though preliminary, and warrants further investigation. 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 head and neck cancer. In 2004, level I evidence was established for the postoperative adjuvant chemoradiotherapy of patients with selected high-risk locally advanced HNC, with the publication of the results of two trials conducted in Europe (European Organization Research and Treatment of Cancer; EORTC) and the United States (Radiation Therapy Oncology Group; RTOG). We are now planning a feasibility study of postoperative adjuvant chemoradiotherapy in patients with high risk locally advanced HNC.

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Average Hospital Stay (Days) in GI Oncology Division (1994-2005)

	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
All cases	35.0 (15)	36.7 (19)	23.9 (10)	17.8 (8)	15.2 (8)	16.7 (9)	14.2 (8)	13.8 (8)	12.3 (7)	13.3 (7)	12.1 (7)	18.6 (8)
Chemotherapy or Palliation case	44.8 (25)	44.4 (31)	28.6 (16)	19.9 (11)	16.8 (9)	17.8 (11)	15.2 (9)	15.1 (10)	13.5 (8)	15.1 (9)	14.4 (8)	18.6 (8)

() : median (days)