

# Hepatobiliary & Pancreatic Oncology

## Introduction

In hepatobiliary and pancreatic cancer treatments, while surgery currently remains the only potentially curative treatment, most patients are found only when the disease is at an advanced and unresectable stage. Clinical trials have therefore been conducted to identify more promising non-surgical treatments for patients with distant metastases or locally advanced disease.

## Hepatocellular Carcinoma

Hepatitis C virus (HCV) is a leading cause of chronic liver disease in Japan; and chronic hepatitis eventually progresses to liver cirrhosis and/or hepatocellular carcinoma (HCC).

Approximate 80% of HCC patients are estimated to be infected with HCV. A multicenter, randomized, placebo-controlled trial of orally administered bovine lactoferrin (bLF) in patients with chronic hepatitis C was conducted to test its efficacy. The primary outcome measure was the virologic response, defined as a 50% or greater decrease in serum HCV RNA level, but there was no significant difference in virologic response rates between the two groups. In conclusion, orally administered bLF does not demonstrate any significant efficacy in patients with chronic hepatitis C (49).

## Biliary Tract Cancer

An early phase II study of uracil-tegafur (UFT) plus doxorubicin, which are approved for biliary tract cancer in Japan, was conducted to investigate the efficacy of this combination regimen in patients with unresectable advanced biliary tract cancer. Three of the 24 patients showed partial responses, and the regimen was well tolerated

(50). Based on these results, a late phase II study involving more than 60 patients was completed in 2006. On the other hand, a registration phase II study of gemcitabine was conducted by Eli Lilly Japan. Seven (17.5%) of 40 patients achieved a partial response. Gemcitabine demonstrated moderate efficacy with manageable toxicity in patients with unresectable biliary tract cancer (51). As a result, gemcitabine was approved for biliary tract cancer in June 2006.

## Pancreatic Carcinoma

In Japan, gemcitabine was approved for treatment of pancreatic cancer in 2001 based on the results of a phase I study. A phase I/II study of combination chemotherapy with gemcitabine and 5-FU was conducted between 2001 and 2002 to improve the efficacy of single-agent gemcitabine against pancreatic cancer. However, a meaningful survival benefit of 7.1 months, over single-agent gemcitabine was not demonstrated (52).

## Clinical Trials

The following trials were completed in 2006.

1. A phase II study of UFT plus doxorubicin for unresectable biliary tract cancer (multi-center study).
2. A phase II study of gemcitabine+S-1 chemotherapy followed by chemoradiotherapy with a radiotherapy dose of 30 Gy for locally advanced disease (single-center trial).  
The following trials are currently in progress.
3. A phase I/II study of S-1 for advanced HCC (multi-center trial); registration trial.
4. A phase II study of systemic chemotherapy with UFT + mitoxantron for advanced HCC (multi-center trial).

5. A phase II study of HAI with CDDP for HCC with portal vein tumor thrombus (multi-center trial).
6. A phase I/II study of HAI with 5-FU, CDDP, and mitoxantrone (FMP regimen) for advanced HCC (multi-center trial).
7. A placebo-controlled randomized phase III study of sorafenib as adjuvant therapy after TACE for HCC (multi-center trial); registration trial.
8. A placebo-controlled randomized phase III study of NIK333 as adjuvant therapy after curative treatment including surgery and ablation therapy for HCC (multi-center trial); registration trial.
9. A randomized phase II study of gemcitabine vs. CDDP + gemcitabine for unresectable biliary tract cancer (multi-center study); registration trial.
10. A phase II study of gemcitabine alone for locally advanced disease (multi-center trial); JCOG study.

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