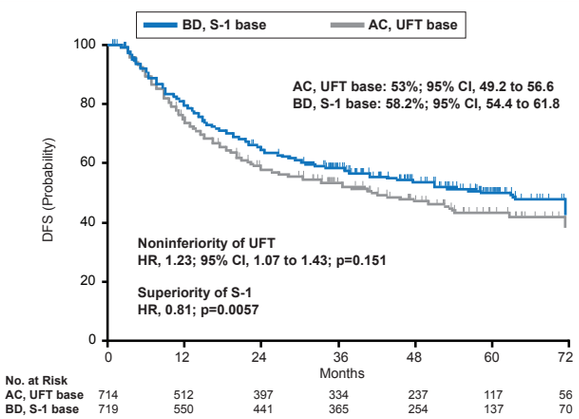
2 weeks Q3W for 16 cycles, 80 mg/m^2 of weekly PAC every 3 or 4 weeks for 1 or 2 cycles, followed by daily UFT Q4W for 9 cycles, or 80 mg/m^2 of weekly PAC every 3 or 4 weeks for 1 or 2 cycles, followed by daily S-1 for 2 weeks Q3W for 12 cycles. All patients had previously undergone R0/1 and extended lymph node dissection. Patients were eligible if they had histologically proven gastric adenocarcinoma stage cT3 or T4, N0-2, or M0, were not previously treated with chemotherapy or radiotherapy, had an ECOG PS of 0 to 1, and were able to begin chemotherapy within 14 to 56 days post surgery.

The median follow-up was 1875 days and the final analysis included 1433 patients, with 359 receiving UFT, 364 receiving S-1, 355 receiving PAC and UFT, and 355 receiving PAC and S-1. The primary endpoint was DFS. Overall survival (OS), compliance, and adverse events were secondary endpoints.

No significant difference in DFS was observed between the UFT and S-1 arms, or the PAC plus UFT and PAC plus S-1 arms. DFS at 3 years occurred in 54% of patients that received UFT or S-1 monotherapy, as compared with 57.2% of patients that received sequential therapy of PAC followed by UFT or S-1 (HR, 0.92; 95% CI, 0.80 to 1.07; p=0.273). However, a number of patients treated with S-1 based therapy (S-1 alone and PAC+S-1) demonstrated 3-year DFS at 58.2%, as compared with 53% of patients that received UFT based therapy (UFT alone and PAC+UFT; Figure 1). This resulted in a HR for noninferiority of UFT of 1.23 (95% CI, 1.07 to 1.43; p=0.151) and an HR of 0.81 for the superiority of S-1 (p=0.0057).

Figure1. DFS at 3 Years Following UFT or S-1 Monotherapy



DFS=disease-free survival; UFT=oral fluoropyrimidine tegafur-uracil.

Reproduced with permission from K Yoshida, MD, PhD.

Similarly, there was no significant difference in OS between the sequential arms. However, the 5-year OS rate was 60.7% in the S-1 based therapy arm compared with 54.3% in the UFT based therapy arm, resulting in a HR of 1.23 for noninferiority of UFT based therapy (95% CI, 1.04 to 1.44; p=0.161).

The most frequent Grade 3/4 adverse events were neutropenia and anorexia. Neutropenia occurred in 11.4% of patients that received UFT monotherapy, 13.2% of patients that received S-1, 13% of patients that received PAC followed by UFT, and 23.4% of patients that received PAC followed by S-1.

Prof. Yoshida concluded that, in his opinion, data from the SAMIT trial indicated that adjuvant treatment of locally advanced gastric cancer with PAC followed by S-1 is safe and effective. However, although treatment with PAC followed by S-1 did not significantly reduce gastric cancer recurrence, there was a trend for improved DFS. In addition, S-1 treatment was demonstrated to be superior to treatment with UFT.

Chemoradiotherapy Fails to Improve Overall Survival in LAPC

Written by Emma Hitt, PhD

Chemoradiotherapy (CRT) is not superior to chemotherapy and the addition of erlotinib provides no benefit in the treatment of locally advanced pancreatic cancer (LAPC). Pascal Hammel, MD, PhD, Hôpital Beaujon, Clichy, France, presented data from the Randomized Multicenter Phase 3 Study in Patients With Locally Advanced Adenocarcinoma of the Pancreas [LAP07; NCT00634725; Hammel P et al. *J Clin Oncol* 2013 (suppl; abstr LBA4003)].

Although not metastatic, LAPC is nonresectable due to the involvement of the superior mesenteric artery and the celiac trunk with tumor. Overall survival (OS) of LAPC is 9 to 12 months, which is greater than that of metastatic pancreatic cancer; however, the treatment of LAPC, including the role of CRT is controversial. The primary objective of the LAP07 study was to determine if CRT improved OS in patients whose disease was controlled following 4 months of induction chemotherapy.

In the international Phase 3 LAP07 study, 442 patients with LAPC and a performance status of 0 to 2 were first randomized to receive gemcitabine (n=223) or gemcitabine plus erlotinib 100 mg/day (n=219) for 4 months. Of the 442 patients, 269 patients (61%) with controlled disease were able to undergo a second randomization to receive 2 additional months of gemcitabine or 54 Gy of CRT plus 1600 mg/m^2 of daily capecitabine. Erlotinib (150 mg/day) was continued as maintenance therapy in patients that had received it during the first randomization.

The median follow-up was 36 months and included 221 deaths, which allowed the interim analysis to be adequately powered. The primary endpoint was OS following the second randomization. The effect of erlotinib on OS,

tolerance of treatment, predictive markers, and presence of circulating tumor cells were secondary endpoints.

In the LAP07 study, CRT was demonstrated not to be superior to chemotherapy in the treatment of LAPC. In the chemotherapy arm, OS was 16.4 months, compared with 15.2 months in the CRT arm (HR, 1.03; 95% CI, 0.79 to 1.34; p=0.8295). Following the first randomization, there was a trend for decreased OS in the gemcitabine plus erlotinib arm at 11.9 months compared with the gemcitabine arm at 13.6 months (HR, 1.19; 95% CI, 0.97 to 1.45; p=0.093); however, this result was not statistically significant.

Following the first randomization, a greater number of patients experienced adverse events such as decreased hemoglobin, febrile neutropenia, diarrhea, and acneiform rash in the gemcitabine plus erlotinib arm, compared with the gemcitabine arm. Following the second randomization, both treatment regimens were well tolerated with a similar frequency of adverse events except for an increase in the number of patients that experienced nausea in the CRT arm (0 vs 6 patients; p=0.009).

Dr. Hammel stated that, in his opinion, the data from the LAP07 trial suggest that the standard of care for the treatment of LAPC should be chemotherapy, with CRT reserved for use as an option if the disease is controlled by chemotherapy. Although CRT or erlotinib provided no additional advantage to patients in the present study, there may be a subset of patients that could benefit, which is currently under investigation.

Targeting Telomerase With GV1001 Vaccine Does Not Prolong OS in Advanced Pancreatic Cancer

Written by Emma Hitt, PhD

Sequential or concurrent treatment with the vaccine GV100 with chemotherapy does not result in a survival advantage in patients with advanced pancreatic cancer. Gary W. Middleton, MD, University of Birmingham, Birmingham, United Kingdom, presented data from the fourth interim analysis of the Gemcitabine and Capecitabine With or Without Vaccine Therapy in Treating Patients With Locally Advanced or Metastatic Pancreatic Cancer study [TeloVac; NCT00425360; Middleton GW et al. *J Clin Oncol* 2013 (suppl; abstr LBA4004)].

Reactivation of the telomerase enzyme is a common mechanism by which cancer cells prevent their senescence and ~80% of pancreatic cancers overexpress telomerase. The GV1001 vaccine targets the hTERT subunit of telomerase that is expressed on the surface of pancreatic cancer cells. In addition, gemcitabine (GEM) has been demonstrated to have immune priming effects that are dependent on the dosing schedule [Nowak AK et al. *Cancer Res* 2003]. The hypothesis of the TeloVac study was that the addition of GV1001 to the current standard of care for advanced pancreatic cancer would provide an overall survival (OS) advantage.

In the multicenter, Phase 3 TeloVac trial, 1062 patients with advanced pancreatic cancer and an ECOG PS of 0 to 2 were randomized 1:1:1 to receive GEM plus capecitabine (CAP); GEM plus CAP followed by GV1001 followed by additional chemotherapy if disease had not progressed by Week 8; and concurrent administration of GEM, CAP, and GV1001.

The median follow-up was 6.11 months and 72.7% of patients died during the study. The primary endpoint was OS. Overall response rate (ORR), time to progression (TTP), and adverse events were secondary endpoints. Prof. Middleton commented that the TeloVac trial was closed following the fourth interim analysis due to declaration of futility.

Administration of GV1001 did not provide a significant benefit when given concurrently or sequentially following GEM and CAP therapy. OS in the sequential GV1001 arm was statistically nonsignificantly inferior at 6.94 months with a 12-month survival rate of 25.3% (HR, 1.19; 95% CI, 0.97 to 1.48; p=0.0466), compared with 7.89 months and 33.7% in the GEM plus CAP arm and 8.36 months and 32.3% in the concurrent arm (HR, 1.05; 95% CI, 0.85 to 1.29; p=0.6378). The ORR was 17.6% in the GEM plus CAP arm (referent), 8.6% in the GEM plus CAP with sequential GV1001 arm (p=0.001), and 15.5% in the concurrent GEM, CAP, and GV1001 arm (p=0.536).

Sequential GV1001 therapy also resulted in a significant inferiority in TTP compared with the other two arms (HR, 1.50; 95% CI, 1.26 to 1.78; p<0.001). The frequency of hematologic and nonhematologic adverse events was similar among each of the treatment arms.

Although GV1001 was well tolerated, it did not appear to provide a benefit in regard to OS, TTP, or ORR. Prof. Middleton pointed out that in the GV1001 sequential arm, progression rates began to increase as soon as patients discontinued chemotherapy for GV1001 treatment, although this did not translate into a significant difference. Immunological analyses, including for predictive biomarkers, are currently ongoing.

Treatment Based on BRCA1 and RAP80 Does Not Extend PFS

Written by Emma Hitt, PhD

Patients that received customized lung cancer treatment based on their levels of BRCA1 and RAP80 did not experience an improvement in progression-free survival