Based on these results, Prof. Rutgers concluded that AxRT can be considered standard treatment for patients with a positive SNB, offering considerably less lymphedema and comparable locoregional breast cancer control with ALND.

Results From the LOGiC Trial

Written by Mary Beth Nierengarten

The addition of lapatinib (L) to capecitabine plus oxaliplatin (Cape/Ox) does not improve overall survival (OS) in patients with locally advanced or metastatic gastric, esophageal, or gastroesophageal junction cancer whose tumors have amplification of the HER2 gene, although an improvement in survival was seen in patients of Asian descent and those aged <60 years.

Results were presented from the Lapatinib Optimization Study in ErbB2 (HER2) Positive Gastric Cancer [LOGiC; NCT00680901; *J Clin Oncol* 2013 (suppl; abstr LBA4001)] by J. Randolph Hecht, MD, University of California, Los Angeles, Los Angeles, California, USA, which compared Cape/Ox alone or in combination with lapatinib (Cape/Ox/L) as first-line treatment for patients with advanced or metastatic HER2 -positive upper gastrointestinal tract cancers.

The Phase 3 trial included 545 patients enrolled between June 2008 and January 2012 from 186 centers in 22 countries. Eligible patients included those with locally advanced or metastatic histologically confirmed adenocarcinoma of the stomach, esophagus, or gastroesophageal junction; measurable or evaluable disease according to RECIST; HER2-positive disease, ≥18 years of age; ECOG PS <2, and no prior palliative chemotherapy.

HER2-positive disease was confirmed in a central laboratory in 487 of the 545 patients by fluorescence *in situ* hybridization. These patients were used as the primary efficacy population (PEP) to evaluate the primary outcome of OS.

Of these 487 patients, 249 were randomized to Cape/Ox/L (oxaliplatin 130 mg/m^2 Day 1, capecitabine 850 mg/m^2 BID Days 1 to 14, and lapatinib 1250 mg QD Days 1 to 21) and 238 to Cape/Ox plus placebo (Cape/Ox/P).

Based on this PEP, the study found no difference in OS between the two treatments with a median OS of 12.2 months and 10.5 months for Cape/Ox/L and Cape/Ox/P, respectively (HR, 0.91; 95% CI, 0.73 to 1.12; p=0.3492).

Under prespecified subgroup analyses, however, significant improvements in OS were seen in Asian patients compared with populations in the rest of the world (ROW) and those aged <60 years. Asian patients had an improvement in median OS from 10.9 months with Cape/Ox/P to 16.5 months with Cape/Ox/L (HR, 0.68; 95% CI, 0.48 to 0.96). The median OS in ROW populations improved from 9.1 for Cape/Ox/P to 10.0 months for Cape/Ox/L (HR, 1.04; 95% CI, 0.79 to 1.37).

Patients aged <60 years also had significantly improved OS compared with those aged ≥60 years, with an improvement in median OS from 9.0 months with Cape/Ox/P to 12.9 months with Cape/Ox/L (HR, 0.69; 95% CI, 0.51 to 0.94). In patients aged ≥60 years, the median OS was 10.9 months with Cape/Ox/P and 11.3 months with Cape/Ox/L (HR, 1.08; 95% CI, 0.81 to 1.45). .

Secondary outcomes of the study showed a progression-free survival of 6 months and 5.4 months for Cape/Ox/L and Cape/Ox/P, respectively, as well as overall response rates of 53% and 40%, respectively, with a median duration of response of 7.3 months and 5.6 months, respectively.

Toxicity was comparable between the two treatment arms, except that Cape/Ox/L was associated with increased overall diarrhea (58%) compared with Cape/Ox/P (29%), Grade 3 diarrhea (12% vs 3%), and skin rash (21% vs 7%).

Based on these results, no improvement in OS was seen with the addition of lapatinib to Cape/Ox except for in Asian patients and those aged <60 years; however, the addition of lapatinib did confer some improvement in progression-free survival and overall response rates.

Sequential Therapy Fails to Extend DFS in Gastric Cancer

Written by Emma Hitt, PhD

There was no significant difference in 3-year disease-free survival (DFS) in sequential treatment of paclitaxel (PAC) and the oral fluoropyrimidine tegafur-uracil (UFT) or paclitaxel and another fluoropyrimidine, S-1, in serosa-invading gastric cancer. Kazuhiro Yoshida, MD, PhD, Gifu University School of Medicine, Gifu, Japan, presented data from the Adjuvant Paclitaxel Followed by Oral Fluorinated Pyrimidines for Locally Advanced Gastric Cancer trial [SAMIT; Yoshida K et al. *J Clin Oncol* 2013 (suppl; abstr LBA4002)].

In Japan, the standard adjuvant chemotherapy for the treatment of gastric cancer was UFT [Oba K et al. *J Chemother* 2006], until results of the ACTS-GC trial resulted in the replacement of UFT by S-1 [Sakuramoto S et al. *N Engl J Med* 2007]. However, Prof. Yoshida pointed out that UFT and S-1 have not been evaluated head-to-head in a clinical trial. In addition, PAC has demonstrated efficacy in advanced gastric cancer. The hypothesis of the SAMIT trial was to demonstrate the superiority of PAC followed by UFT or S-1 compared with no PAC use and the noninferiority of UFT to S-1.

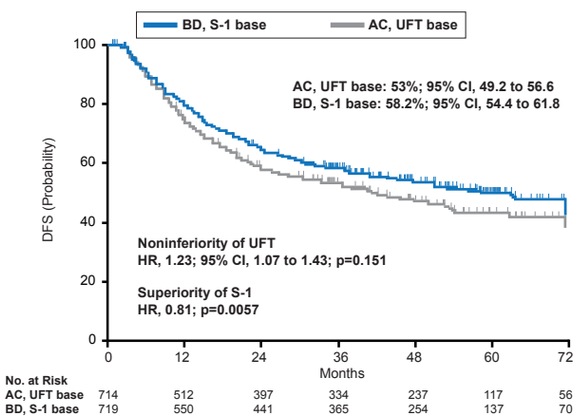
In the multicenter, Phase 3 trial, 1495 patients with serosa-invading gastric cancer were randomized with a 2x2 factorial design to receive 267 mg/m^2 of daily UFT alone Q4W for 12 cycles, 80 mg/m^2 of daily S-1 alone for

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.

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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,